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Quantitative Relations in the Physiological Constitutions of Mammals

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THE INVESTIGATION OF VITAL FUNCTIONS customarily ends with the establishment of a relation between process X and process Y. It need not end so; and the object of the present paper is to show how the relations may be multiplied, providing either X or Y is used as a common correlative in further studies.

Most data of physiology concern the rates of processes. The rates represent the events, regardless of the manner in which the processes are performed. By measuring the ordinary events of living in several species, or in several individuals of diverse sizes or activities, the disproportionalities among processes are disclosed. The present description is limited to correlations *among* species and chiefly to data upon mammals. The result illustrates a quantitative method in comparative physiology and in generalized physiology.

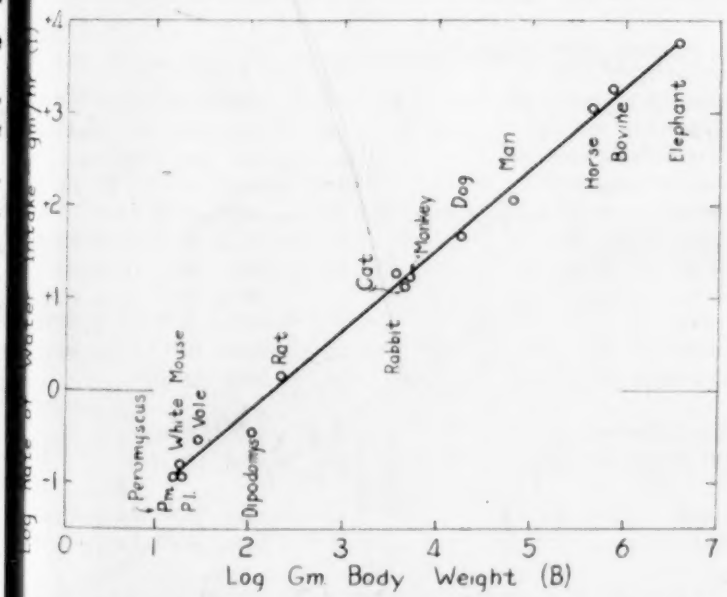

FIG. 1. Rate of water intake (I) in relation to body weight (B) among species of mammals. $I = .010\ B^{.88}$. From Adolph (*1*, p. 270).

In a previous study, rates of water exchanges were correlated with body sizes among mammals (*1*, p. 270). One set of those data is reproduced in Fig. 1. It is evident that logarithms of water intakes (I) are proportional to logarithms of body weights (B). The data fit an equation:

$$I = aB^k \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (I)$$

which may also be written:

$$\log I = \log a + k \log B \quad . \quad . \quad . \quad . \quad (II)$$

The coefficients a and k can be ascertained from the graph or by computation of least squares. Such power equations have been widely found to express suitably the regressions between organ sizes, and to a more limited extent to relate rates of oxygen consumption with body sizes (*3*).

The empirical relation of Fig. 1 turned out to be

$$I = .010B^{.88} \quad . \quad . \quad . \quad . \quad . \quad (III)$$

The exponent means that water turnover (ml/hr) is not proportional to body weight (g); if it were, the exponent would be 1. The larger mammals have, relative to weight, less turnover than the smaller, and many suggestions have been put forward to the effect that rates of diverse processes might be proportional to body surface areas, perhaps to $B^{.67}$, or to other power functions of B. The general form of this equation is referred to as heterogonic; it expresses degrees of disproportionality; it is an equation of similitude. In a group of such equations might be implicit most of the factors by which an elephant differs from a mouse.

From the same source (*1*, p. 271) data are available relating urinary outputs (U) to body weights (B) in mammals. In this case,

$$U = 0.0064\ B^{.82} \quad . \quad . \quad . \quad . \quad . \quad (IV)$$

Evidently urine production is slightly more disproportional to body weight than is water intake. The relation implies that small animals (as compared with large animals) lose a slightly smaller fraction of their water turnover by paths other than urinary excretion; the chief other path of loss is evaporation.

The interrelation can be more clearly expressed by the appreciation of the fact that since I and U are each related to B, they are related to each other. Or, more generally,

$$Y = a_1 X^{k_1} \quad . \quad . \quad . \quad . \quad . \quad . \quad (V)$$

and

$$Z = a_2 X^{k_2} \quad . \quad . \quad . \quad . \quad . \quad . \quad (VI)$$

or

$$\log X = \frac{\log Y - \log a_1}{k_1} = \frac{\log Z - \log a_2}{k_2} \quad . \quad (VII)$$

then

$$\log Y = \log a_1 + \frac{k_1}{k_2} (\log Z - \log a_2) \quad . \quad (VIII)$$

and

$$Y = a_1 \left(\frac{Z}{a_2}\right)^{\frac{k_1}{k_2}} \quad . \quad . \quad . \quad . \quad . \quad (IX)$$

In the specific instance of I and U,

$$\log I = \log .010 + \frac{.88}{.82} (\log U - \log .0064) \quad . \quad (X)$$

$$= -2.000 + 1.073 (\log U + 2.194) \quad . \quad (XI)$$

or

$$I = 2.25\, U^{1.073} \quad . \quad . \quad . \quad . \quad . \quad (XII)$$

The inverse of relation IX has the form

$$Z = a_2 \left(\frac{Y}{a_1}\right)^{\frac{k_2}{k_1}} \quad . \quad . \quad . \quad . \quad (XIII)$$

from which

$$U = .46\, I^{.93} \quad . \quad . \quad . \quad . \quad . \quad (XIV)$$

and the inverse of relation V has the form

$$X = \left(\frac{Y}{a_1}\right)^{\frac{1}{k_1}} \quad . \quad . \quad . \quad . \quad . \quad (XV)$$

These expressions of quantitative interrelations may be applied to all functions in which log Y is proportional to log Z. Other expressions can be utilized to express interrelations when additional forms of disproportionality may be found.

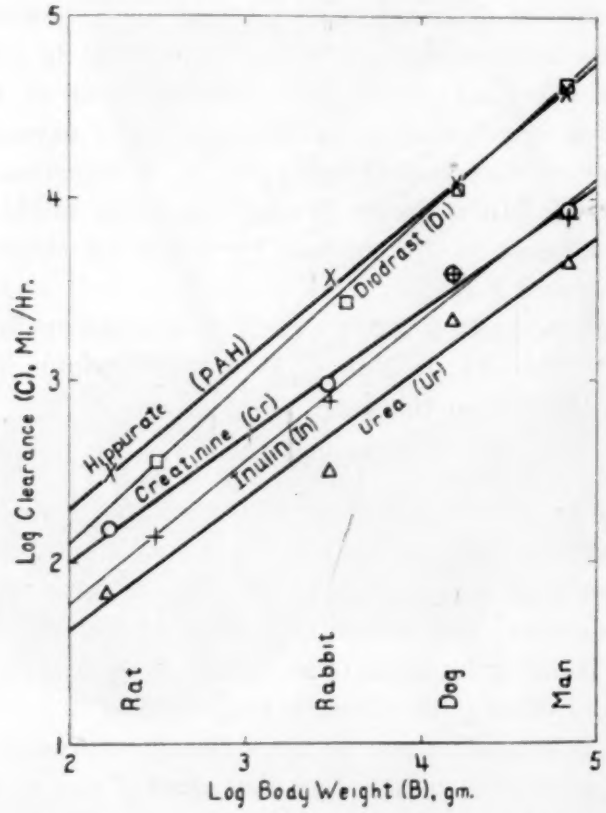

FIG. 2. Renal clearances (C) in relation to body weight (B). Straight lines are fitted on log-log units by least squares from points established for maximal clearances. Rat—Lippman, Dicker, Dicker and Heller (*19, 7, 8*). Rabbit—Kaplan and Smith, Forester and Maes, W. W. Smith (*16, 11, 25*). Dog—Dominguez, Houck, Moustgaard (*9, 15, 22*). Man—Hayman *et al.*, Goldring *et al.*, Chasis *et al.* (*14, 12, 4*).

Since a great many data of anatomy, biochemistry, and physiology can be shown to fit the heterogonic equation, the fruitfulness of this particular form of relation may be illustrated from them.

Renal clearances, which are measurements of excretory functions, have been ascertained for single organic substances in several species; their magnitudes are related with the body weights of those

TABLE 1

EQUATIONS RELATING QUANTITATIVE PROPERTIES WITH BODY WEIGHTS AMONG MAMMALS*

Intake of water (ml/hr)	I	$=.010\ B^{.88}$ (Fig. 1)
Urine output (ml/hr)	U	$=.0064\ B^{.82}$ (*1*, p. 271)
Urea clearance (ml/hr)	C_{ur}	$=1.59\ B^{.72}$ (Fig. 2)
Inulin clearance (ml/hr)	C_{in}	$=1.74\ B^{.77}$ "
Creatinine clearance (ml/hr)	C_{cr}	$=4.2\ B^{.69}$ "
Diodrast clearance (ml/hr)	C_{di}	$=2.14\ B^{.89}$ "
Hippurate clearance (ml/hr)	C_{PAH}	$=5.4\ B^{.80}$ "
O_2 consum. basal (ml STP/hr)	O	$=3.8\ B^{.734}$ (*3*, p. 370)
Heartbeat duration (hr)	H	$=.000\ 0119\ B^{.27}$ (*5*, p. 89)
Breath duration (hr)	Q	$=.000\ 047\ B^{.28}$ (*13*)
Ventilation rate (ml/hr)	V	$=120\ B^{.74}$ (*13*)
Tidal volume (ml)	T	$=.0062\ B^{1.01}$ (*13*)
Gut beat duration (hr)	G	$=.000\ 093\ B^{.31}$ (*5*, p. 91)
N Total output (g/hr)	N_T	$=.000\ 074\ B^{.735}$ (*3*, p. 377)
N Endogenous output (g/hr)	N_B	$=.000\ 042\ B^{.73}$ (*3*, p. 377)
Creatinine N output (g/hr)	N_{cr}	$=.000\ 001\ 09\ B^{.90}$ (*3*, p. 378)
Sulphur output (g/hr)	S	$=.000\ 001\ 71\ B^{.74}$ (*3*, p. 378)
O_2 consum. liver slices (ml STP/hr)	O_L	$=3.3\ B^{.77}$ (*28*)
Hemoglobin wt (g)	H_b	$=.013\ B^{.99}$ (*10*)
Myoglobin wt (g)	M_y	$=.000\ 039\ B^{1.31}$ (*10*)
Cytochrome wt (g)	P_c	$=.000\ 10\ B^{.84}$ (*10*)
Nephra number	N	$=2600\ B^{.62}$ (Fig. 3)
Diameter renal corp. (cm)	D	$=.0081\ B^{.08}$ (*18*)
Kidneys wt (g)	K	$=.0212\ B^{.85}$ (*3*, p. 625)
Brain wt (g)	E	$=.081\ B^{.70}$ (*3*, p. 592)
Heart wt (g)	J	$=.0066\ B^{.98}$ (*3*, p. 596)
Lungs wt (g)	F	$=.0124\ B^{.99}$ (*3*, p. 627)
Liver wt (g)	L	$=.082\ B^{.87}$ (*3*, p. 626)
Thyroids wt (g)	M	$=.000\ 22\ B^{.80}$ (*3*, p. 621)
Adrenals wt (g)	A	$=.0011\ B^{.92}$ (*3*, p. 585)
Pituitary wt (g)	P	$=.000\ 13\ B^{.76}$ (*3*, p. 596)
Stom. + intes. wt (g)	W	$=.112\ B^{.94}$ (*3*, p. 628)
Blood wt (g)	R	$=.055\ B^{.99}$ (*3*, p. 593)

* Source of equations or data from which equations have been derived are indicated. All values are in ml, g, cm, and hr.

species (Fig. 2). A clearance is a ratio between a rate of disposal of a substance (g/hr) and its concentration in body fluid (g/ml). The data here represented have been selected by the sole criterion of taking, within each species, the arithmetical mean of that series of measurements giving maximal values for clearance of each substance. Evidently the several substances are not cleared in proportion to the body weight; the equations all have exponents less than 1. There is no support for the guess that all the

exponents are alike, or, as many physiologists assume, that all are .67. Within one species it may well be that measurement of one clearance foretells all the others; but different proportions evidently prevail within different species. The relations from which such predictions may be formulated are listed in the

TABLE 2

EQUATIONS INTERRELATING SOME QUANTITATIVE PROPERTIES OTHER THAN BODY WEIGHT, DERIVED FROM TABLE 1*

$U = .46\ I^{.93} = .0108\ C_{ur}^{1.14} = .000{,}000\ 19\ N^{1.32}$
$C_{ur} = .35\ C_{PAH}^{.90} = 17{,}700\ N_T^{.98} = 42\ K^{.85}$
$O = 1300{,}000{,}000{,}000\ H^{2.72} = 11{,}900\ P^{.87}$
$V = 370{,}000{,}000{,}000{,}000\ H^{2.74} = 4900\ T^{.73}$
$N_T = .0068\ U^{.90} = 5.4\ N_{cr}^{.82} = .000{,}0162\ C_{cr}^{1.06}$
$O_L = 30\ L^{.89} = .81\ O^{1.05} = 1290\ M_y^{.59}$

* All values are in ml, g, cm, and hr.

equations of Table 1; one of them is given as an example in line 2 of Table 2.

A very large number of relations between physiological rates taken two at a time becomes available. A limited set of data relating each function to body weight (Table 1) allows its relations with other quantities to be expressed in the manner of Table 2 without need for new measurements. Indeed, the relationships once ascertained on several species of diverse sizes will establish a relation that may then be used to describe the relationships established by the study of entirely different species. Thus, the data

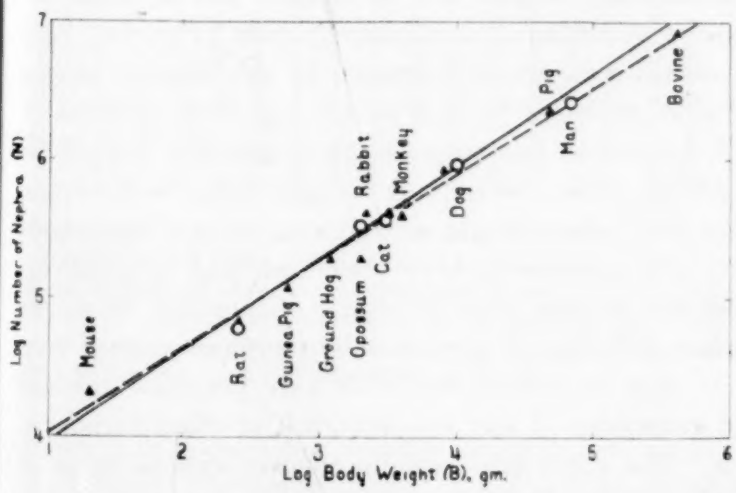

FIG. 3. Number of nephra (N) in two kidneys in relation to body weight (B) among mammals. The solid line ($N = 1900\ B^{.67}$) fits the circles which represent on log-log scales the arithmetical means of counts of glomeruli made by Arataki (*2*) for rat, Nelson (*23*) for rabbit, Vimtrup (*26*) for cat and dog, Moritz and Hayman (*20*) for man. The dotted line ($N = 2600\ B^{.62}$) fits the triangles, which represent arithmetical means of counts made by Kunkel (*18*).

of Fig. 1 might have been obtained solely from mouse, cat, horse, and elephant; those of Fig. 2 being derived from four other species. Nevertheless the relation between I and C_{ur} would evidently be derived with almost the same degree of determination as by the use of identical species for both measurements.

From the reservoir of data upon numerical relationships of structural peculiarities to body sizes, specifically interesting relations with physiological rates may be derived. For instance, the number of nephra in the kidneys of various mammals have been counted; the numbers relate to body sizes (Fig. 3) with heterogony of low power (.62). Then urinary flow, having a higher power in relation to body weight (.82) has an exponent 1.32 in relation to nephra number. This means that when the number of excretory units is 10-fold as great, the rate of urinary excretion is 21-fold as great. In the bovine each nephron puts out 52 times as much urine as in the rat. The diameters of renal capsules increase only slightly with body weight (exponent .08). However, the volumes of renal corpuscles increase with body weight as the exponent .24. Hence the physiological activity of each nephron turns out to have a markedly different magnitude among species; but each unit of volume of renal corpuscles is about proportional to urinary flow, since

$$ND^3 = a\ B^{.86} \quad . \quad . \quad . \quad . \quad . \quad \text{(XVI)}$$

and each unit of surface,

$$ND^2 = a\ B^{.78} \quad . \quad . \quad . \quad . \quad \text{(XVII)}$$

Similarly, the renal clearance of none of the five substances (for which data are presented in Fig. 2) is proportional to nephra number. A nephron in a bovine, approximately identical in structure with that of a mouse, clears more of each excretory substance. Realization of this fact might lead to extensive search for differences among nephra.

A few data upon rates of excretion of solutes have been analyzed in relation to body weights by Brody (Table 1: N_T, N_E, N_{cr}, S). One fact here discovered is that creatinine excretion is not proportional to creatinine clearance among species.

Correlations among physiological processes need not be restricted to processes that utilize in large part any one organ (kidneys) or any one activity (excretion). It is equally useful to find the interrelations among processes that have scarcely been thought of as being interrelated. To the above excretory processes may, therefore, be related basal oxygen consumption (*3*), duration of heartbeat (*5*), duration of one intestinal contraction (*5*), duration of one breath (*13*), respiratory ventilation rate, and tidal volume. All three of the above durations have the property of being correlated with body weight (Table 1) by low exponents. Their reciprocals (frequencies) are negative correlatives of body weight.

Data are available for intercorrelations with the above quantitative properties, in the rates of oxygen

consumption of tissue slices (O_L) obtained from homologous organs of several species (Table 1). Interest has centered in the fact that these consumptions per unit of tissue *weight* vary as negative powers of body weight (*28*), for that fact indicates that the properties by which large animals consume less oxygen per gram of weight are impressed in their tissues even after isolation. Here these relations are expressed in the form

$$O_L = a\,B^k \quad . \quad . \quad . \quad . \quad \text{(XVIII)}$$

instead of

$$O_L/B = a\,B^{k-1} \quad . \quad . \quad . \quad . \quad \text{(XIX)}$$

Many physiologists are aware that oxygen consumption is proportional (i.e., with exponent 1) to ventilation rate. (Guyton's data [*13*] yield the constant $O = .028\,V$); and some recognize that oxygen consumption is proportional to nitrogen output (Brody's data [*3*] show that $O = 52{,}000\,N_T$). Further, ventilation rate is proportional to nitrogen output ($V = 1850\,N_T$). These three quantities share the exponent 1 in their relations to one another. In a species where one or two of the three are difficult to measure, they may be computed from the third (or from any of the 33 correlatives represented in Table 1).

A number of biochemical correlations may be estimated from extant data. Concentrations of cytochrome *C* diminish with increased body size (*10*) and suggest thereby a basis for lesser oxygen consumptions per unit tissue mass. To date, most biochemical studies have been limited to one species at a time, and little consideration has been given to the known diversities of composition among species and the implications of those diversities. The interspecific relations here derived may now be regarded in turn as definite functions of all the physiological characters mentioned.

Anatomical characteristics may be added to the total picture. Those that possess known disproportionalities to body weight (Table 1) may have their disproportionalities toward one another computed. The interrelations to function may be illustrated in the weights of kidneys, which are definitely not proportional to many of the clearances and rates of excretion presented above. Altogether, from the 33 equations of Table 1 may be derived 33×32 or 1056 equations expressing relations between two properties at a time. Those given in Table 2 are only a few samples. Each of the 1056 has an inverse equation XV.

Alternative sets of data that may confirm any of the above equations are few. For basal oxygen consumptions, the equation $O = 3.8\,B^{.72}$ is computed for rodents of 11 species from data of Morrison (*21*). Weights of seven visceral organs have been analyzed from 20 species of ungulates of diverse sizes by Quiring (*24*), which could replace the corresponding equations of Table 1. Among these seven organs only brain and heart had significantly different (smaller) coefficients than among the corresponding organs analyzed by Brody (*3*). With sufficient measurements it might be, as Morrison's data (*21*) suggest, that diverse orders of mammals will have diverse coefficients of regression in bicorrelations of their properties. It might also turn out that taxonomic orders based upon physiological properties will not segregate species in the same groupings as they are assigned by taxonomists.

There is no reason other than nonavailability for limiting the data mentioned to the physiological properties of mammals. Beginnings have been made in gathering data concerning the oxygen consumptions of diverse crustacea (*29*) and mollusks (*27*) and for water exchanges of aquatic animals generally (*1*, p. 272), as related to body sizes. It must be recognized that no limitation is imposed, by anything but the time and effort of investigation, upon the range of organisms and upon the array of properties that may be considered in interrelations.

A similar analysis may be applied to the changes (growth) in functions during the successive ages of organisms of any one species, or within any one individual.

The fact that all of the properties listed in Table 1 are equally related one to another can be made explicit by means of an alignment chart (Fig. 4). Each vertical scale was constructed by substituting integer values of log Y in each of the equations of Table 1. A horizontal line connects all values that belong together. There is nothing unique about body weight or any other single correlative, except that body weight happens to have been measured in gathering all the original measurements. From this chart, the characteristics of a mammalian organism, such as a cat, can be ascertained with fair precision through a knowledge of any one quantitative characteristic of it. The chart also permits comparisons to be made between any two or more species, as between cat and mouse. One would note, for instance, the great ratio of tidal volumes (T) of the two species, but the small ratio of breath durations (Q). Insofar as mean data can be utilized to describe a species, this chart is valid. For species not yet investigated, predictions are furnished by it. It allows of a probable reconstruction of the characteristics of species now extinct.

Some physiologists will hesitate to extrapolate from the data upon which the equations of Table 1 and the scales of Fig. 4 are based. A few will also hesitate to interpolate in certain zones.

Fig. 4 condenses an enormous amount of information and inference about mammals, since it represents not only 34 biological characteristics in potentially hundreds of species, but also the interrelations among all of them. The appreciation of the myriads of diverse interrelations cannot be made explicit here.

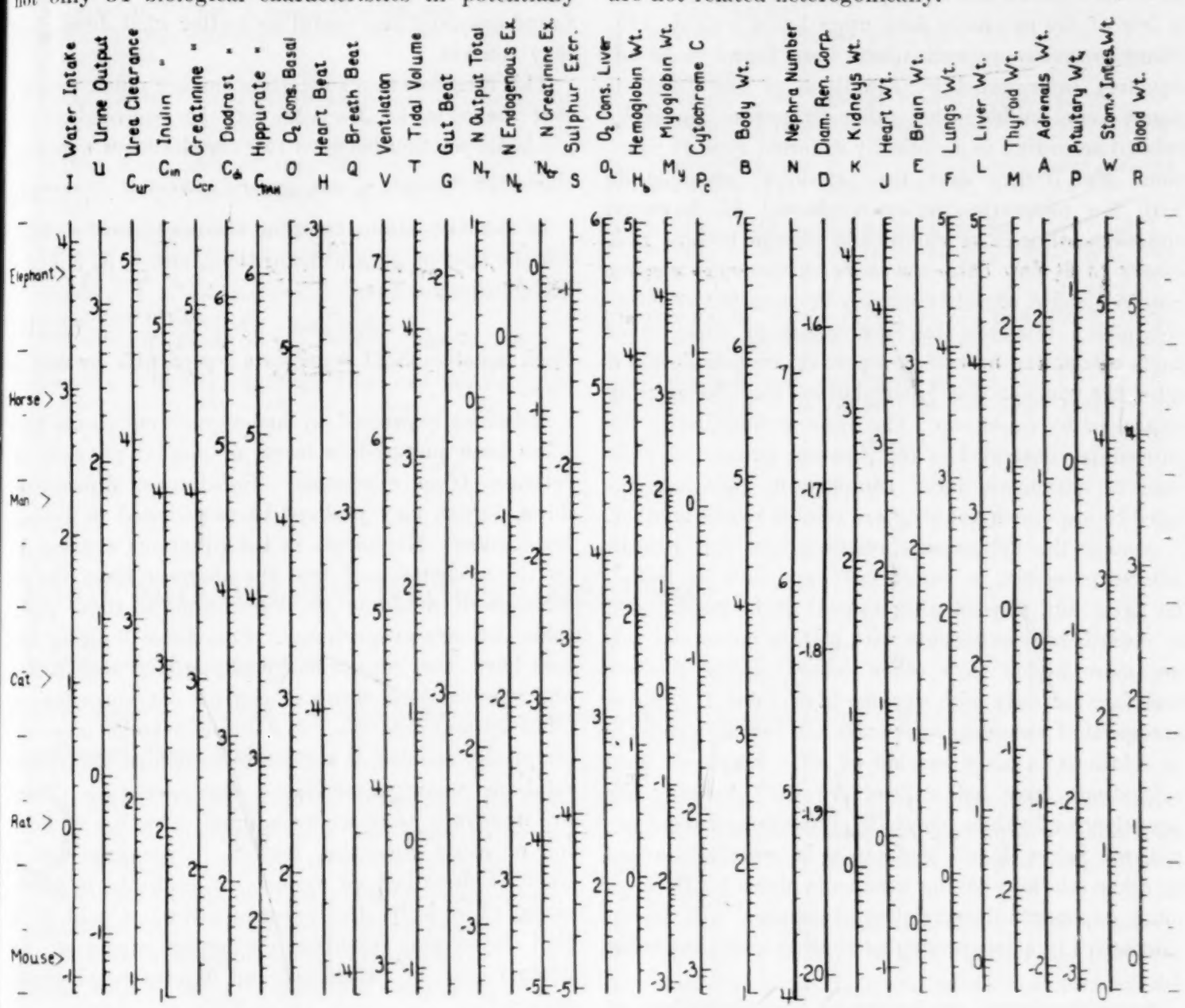

FIG. 4. Alignment chart exhibiting the relations among 34 properties of mammals. The characteristics of one animal are read off along a horizontal thread or ruler that is placed at a known value in any one of the variables. Several species chosen at random are indicated on the left at their appropriate scale positions. Ordinates are numbered as exponents of 10; but the subdivisions between ordinates read arithmetically. Thus, the number 1 means 10^1 and the subdivisions above it mean 20, 30, 40, etc. All values are in ml, g, cm, and hr, as shown in Table 1. The lines and scales represent, and are derived from, the equations of Table 1.

Coefficients of correlation between diverse properties are best computed not from intraspecies means but from single measurements. The correlation coefficients (r) found among some of the functions here named are high; many for instance are 0.95 (see Brody, *3*). The corresponding coefficients of determination (r^2) are therefore 0.90; or in ordinary parlance, process X goes with Y to the extent of 90 percent. The high "determination" is not exclusive, and many other processes are equally highly correlated with both X and Y. The remaining 10 percent allows plenty of latitude for those species peculiarities that are not related heterogonically.

Many physiological properties go hand in hand with one another; their "determination" is reciprocal and not unique. It seems likely that an organism is an integrated system by virtue of the fact that none of its properties is entirely uncorrelated, but that most are demonstrably interlinked; and not just by single chains, but by a great number of crisserossed linkages.

General comment. The heterogonic or power equation is only one of many conceivable equations which might be empirically found to express the regressions between rates of physiological processes. Among organ sizes and biochemical constituents, however, it is

the only one that has been found to apply to a large number of relations. The only interspecies data that have been shown not to fit precisely this equation are a few of the extensive data upon brain weights (*6*). Since so many properties have been found to be adequately interrelated by equations of one form, it seems very unlikely that other properties would be related according to a radically different type of equation. For if they were, they would be incompatible with the properties reviewed above. If, however, equations of greater complexity should become necessary to fit new data, the more cumbersome algebra required might impede the study of quantitative interrelations. Whether the heterogonic or some other form of relation between properties prevails does not alter the concept that interrelations may be usefully expressed by equations. The basic assumption in the procedure illustrated is that, among properties common to organisms under comparison, quantities related to a common quantity are related to one another.

Among the heterogonic relationships that prevail among processes, a variety of exponents is found. By tradition, physiologists appear to be conditioned to regard those exponents with certain numerical values more highly than other values. Some persons feel familiar only with exponents of value 1. Others assume that processes in general will reveal exponents in relations to body weights of .67. Empirical considerations have led still others (*17*) to note the prevalence of values about .75. Relations having exponents below 1 will ordinarily be counterbalanced by other relations having exponents above 1. Perhaps most exponents interrelating processes will group themselves in a frequency distribution about the value 1.

Some properties are known to be independent of body sizes (e.g., basal alveolar pressures of carbon dioxide). They are nonetheless connected with properties (such as basal ventilation rates) that are dependent upon body sizes among species.

For every heterogonic exponent below 0, its reciprocal is obviously above 0, and of the same numerical value: that is

$$\frac{1}{Y} = \frac{X^{-k}}{a} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (XX)$$

For every negative exponent, then, some related quantity has a positive exponent. Thus, the reciprocal of heartbeat frequency is beat duration. Only by thinking of those two measurements as separable can anyone suppose that the exponent for the frequency is more "important" than the exponent for its reciprocal, the duration.

Use of the heterogonic equations in as general a manner as they are here applied is justifiable from the aspect of their dimensions because the coefficient a takes its dimensions from those of Y and X. Since the equations were derived empirically the relations found are valid and useful no matter what dimensions they contain.

This consideration suggests a further point, namely, that the equation $Y = a X^k$ may be regarded as the algebraic relation between two simultaneous exponentials such as

$$Y = be^{-\beta t} \text{ and } X = ce^{-\gamma t} \quad . \quad . \quad . \quad . \quad (XXI)$$

In these equations the time t is concurrent in both, e is the base of natural logarithms, and b, β, c, and γ are constants. Then

$$k = \beta/\gamma \text{ and } a = b/c^{\beta/\gamma} \quad . \quad . \quad . \quad (XXII)$$

Each equation XXI represents a separable process in time.

Relations expressed by heterogonic equations have often been pictured in terms of special physical inferences from exponents. Substances, dimensions, flows, forces, may perhaps be partitioned in a regular manner. Exponents in the equations express the partitions found, and free the observer from the restriction of confining his descriptions to those partitions that are proportional. Sometimes limiting factors have been conceived for these flows and forces, and specifically in terms of enzyme concentrations or other special controls. For those persons more descriptively minded, it suffices to recognize the orderly relations among quantitative characteristics. There are numerous cases where nothing is known of limiting or other governing factors. Organisms can at least be described as systems of multiple interrelations, of orderly disproportionalities. Could it be that heterogony expresses a major aspect of the ground plan of functional and of structural constitutions?

In summary, interrelations are derived, by use of the heterogonic equation $Y = a X^k$, from specific data representing the rates of particular physiological processes. The exponent k expresses the relative rates of X and Y as found by measurements, and for purposes of illustration data available for mammals of diverse species have been analyzed. The interrelations found imply quantitative orderliness among characteristics so diverse as urinary flow, renal clearance, duration of heartbeat, and oxygen consumption. Organisms may be pictured as systems of precise multiple interrelations. These interrelations apply not only to rates of physiological processes, but also to sizes of organs, numbers of reduplicated structures, and biochemical compositions. Some 34 correlatives in mammals are presented nomographically so that from a measurement of any one property the 33 others can be read.

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Detail and Survey Radioautographs[1]

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QUASI-MICROSCOPIC TECHNIQUES in radioautography have left much to be desired in the study of the cellular distribution of radioactive elements and labeled compounds (*19*). The introduction of nuclear track emulsions in radioautographic techniques (*8*) has brought with it the possibility of studying localization of radioactive substances at oil immersion magnification. Alpha tracks have been studied at high magnification (*1, 8*) in conjunction with soft tissue sections mounted on the emulsion (*8, 9*). The localization of beta emitters has been studied at high magnification in tissue sections and blood smears (*5, 6*). The principles of radioautographic technique have been reviewed recently (*1, 4, 10, 11*) and techniques for special purposes have been described (*3, 5, 13, 14, 17*).

The much used *survey* or *contact* type of radiograph (*2, 12*) illustrated in Fig. 1 is indispensable for a study of the gross distribution of radioactive materials. This figure shows the distribution of plutonium in the tibia of a young rat. The section was cut unsoftened (*15*) at 10 μ. The survey examination, however, gives only the gross picture and does not reveal directly the detailed localization of this heavy metal.

A *detail* radioautograph is equally indispensable. Its application to bone is seen in Fig. 2, which was prepared by mounting a second thin section of the tibia on nuclear track emulsion. The detail radioautograph makes it possible to determine the localization of plutonium with respect to cells.

The interpretation of a detail radioautograph depends upon the determination of the point of origin of the emission. Although this is far more easily accomplished for alpha particle emitters, as in Fig. 2, much information may be obtained by examining at high magnification a beta particle sensitive nuclear track emulsion (*5, 7*). A description of the types of nuclear tracks is given by Powell and Occhialini (*18*).

Nuclear particles leave their points of origin in the tissue and travel in random directions. About half of the particles enter the emulsion and strike silver grains. The series of grains in a single path, when developed, reveal a nuclear track (A, Fig. 2). The mean free path is determined by the type and energy of the emission. Thus, the track can be retraced towards the locus in the tissue from which it origi-

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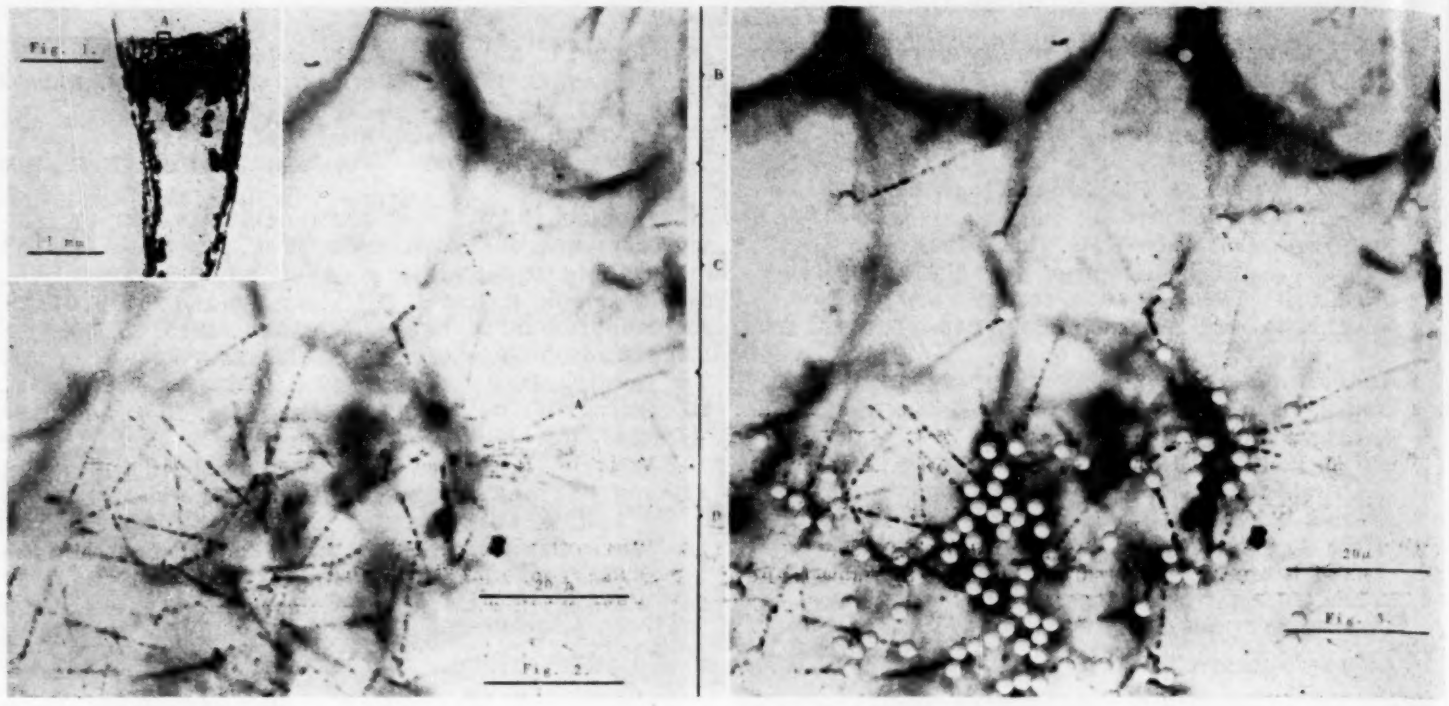
[2] Grateful acknowledgment is made to Mrs. Julie Wellnitz and Mrs. Norma Lanter for technical assistance.

[3] On leave from Washington University School of Dentistry.



Section of tibia of 9-day-old Wistar rat, 16 g, injected intraperitoneally at 7 days of age (approx. 10 g) with 5.9 μg plutonium as citrate. Ten-μ sections of unsoftened bone (Rat 13; spec. 133; embedded in nitrocellulose, R.S. ½ sec). Fig. 1 shows a *survey* radioautograph, by contact with Eastman ultra-speed dental X-ray film, exposed 31 days. *A*—indicates area of the *detail* radioautograph. (Pl. 001494.) Fig. 2 shows a *detail* radioautograph, tissue section mounted on Eastman NTA plate, exposed 7 days. *A*—Alpha track (tissue end in focus); *B*—zone of vesicular cartilage cells (tissue plane out of focus); *C*—zone of eroded cartilage cells; *D*—primary spongiosa. (Plate 063; stained with hematoxylin eosin; Bausch and Lomb Ampliplan 6, Zeiss oil immersion apochromatic 60; extension of camera 50 cm.) Fig. 3 shows localization of plutonium, in the *detail* radioautograph of Fig. 2, marked by placing map tacks at the tissue end of each nuclear track. Note the orderly distribution of plutonium as against the apparent haphazard arrangement of tracks seen in Fig. 2. (Pl. 001496.)

nated by focusing up and down with the fine adjustment of the microscope at high magnification. For purposes of orientation the points of origin may be marked on an enlarged photomicrograph with map tacks. As marker after marker is placed at the beginning of the tracks the pattern of localization of the radioactive substance can be visualized. The orderly localization of plutonium in the region of the zone of eroded cartilage cells of the tibial epiphysis is shown in Fig. 3.

Outlines of survey and detail radioautographic techniques are given in Table 1. The necessity for the use of pressure to insure intimate contact between tissue and emulsion for *survey* radioautographs has been demonstrated by Sherwood's studies (*20*) of microradiographic technique. Nitrocellulose sections are mounted on nuclear track plates by carrying a flat section wet with approximately 75 percent alcohol on a section lifter to the emulsion. The water and alcohol render the gelatin surface sticky enough to hold the section securely throughout processing. The section is quickly covered with filter paper (Whatman's No. 1) and the excess alcohol is taken up by moving a tissue roller back and forth over the plate. The nitrocellulose is immediately removed by repeated flooding with ether-alcohol.

Selection of the emulsion is greatly simplified by an understanding of the functions of the survey and detail radioautographs. For survey radioautographs large grain size is not objectionable. Even the shortest tracks, such as those from an alpha particle, may

TABLE 1

OUTLINE OF RADIOAUTOGRAPHIC TECHNIQUE

	Survey radioautograph	*Detail* radioautograph
	Contact	
Mount:	*Mount* tissue on microscope slide (stain after radioautographic exposure). *Place* film against tissue. *Wrap* appropriately to prevent scatter to next film. *Clamp* between glass slides with two 7-lb paper clamps. *Expose* in box, painted black inside and out (*5*).	*Mount tissue on emulsion.*
Emulsion:	*Fast X-ray film.*	Alphagraph: Alpha or beta sensitive *nuclear track emulsion.* Betagraph: Beta sensitive *nuclear track emulsion.*
Exposure:	*Estimate* exposure time from experience with comparable material.	Approximately ⅓ exposure time of survey radioautograph.

radiate a distance of 20 μ. Thus, the total width of the radioautographic image of a point source of alpha particles may be as great as 40 μ (*4*). For beta emitters the images will be much wider (*4, 16*). Therefore, since the fastest emulsions have a grain size sufficiently small to show all the detail possible by the contact radioautographic technique, the selection of an emulsion is determined by the emulsion speed desired. Fast X-ray films offer the advantage of the shortest possible exposure time for survey radioautographs. *Processing* of the emulsions must be carried out according to the manufacturers' recommendations.

In summary, radioautographic examination of thin tissue sections is accomplished by two complementary procedures. Survey radioautographs may be obtained by the well-known method of pressing the tissue, mounted on a glass microscope slide, in contact with a fast X-ray emulsion. Detail radioautographs for examination at high magnification under high dry and oil immersion objectives may be obtained by recently announced methods in which the section is *mounted directly on a nuclear track emulsion.*

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TECHNICAL PAPERS

A New Group of Plant Growth Regulators

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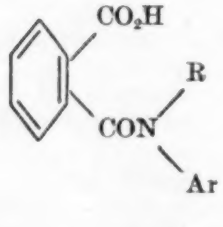
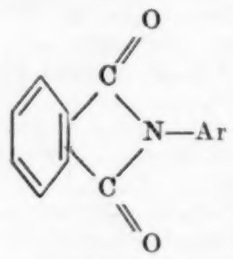
A new group of plant growth regulating chemicals, the N-aryl phthalamic acids, has been discovered. These compounds, which are readily prepared from phthalic anhydride and aromatic amines, can be represented by the general formula I. The esters, amides, and soluble salts of these acids, as well as the N-aryl phthalimides (II) have been found to possess similar activity.

I



II



Where R is a hydrocarbon radical or a hydrogen atom, and Ar is an aromatic group.

The nature and degree of the growth response shown by plants treated with these chemicals depend on the type and age of the plant, and on the concentration and identity of the phthalamic acid derivative used. Data from a field test in which Bonny Best tomato plants having from one to three unset blossom clusters were treated with compounds of this group show the effects obtained (see Table 1). Each plant was sprayed with 100 cc of a solution containing one drop of a commercial wetting agent (Emulphor EL) per 100 mg of chemical used.

TABLE 1

N-aryl phthalamic acid Aryl group	Approximate minimum concentration in ppm to cause: Chemical fruit set	Formative effect	Pronounced inhibition of fruit set
2-Chlorophenyl	63	20	632
2,5-Dichlorophenyl	63	200	632
2,4,5-Trichlorophenyl	63	632	632
3-Chlorophenyl	63	632	632
4-Chlorophenyl	63	632	200
4-Bromophenyl	200	632	632
o-Tolyl	200	632	2000
4-Nitrophenyl	200	2000	2000
2-Nitrophenyl	632	2000	*
2-Hydroxyphenyl	632	632	*
m-Tolyl	632	632	*
p-Tolyl	2000	200	*
Phenyl	2000	*	*

* The effect was not produced at 2000 ppm, the highest concentration tested.

It will be seen that the active concentrations of different compounds vary greatly. A general pattern of response, however, is evident. At low concentrations fruit set is stimulated, and seedless tomatoes are often produced. A morphological response involving a broadening of the leaves is usually evident. This formative effect does not appear to injure the plant seriously; in fact, in some cases the test plants actually seemed to be more vigorous than the unsprayed check plants.

As the concentration of chemical is increased, the formative effect becomes more pronounced. Fruit set is inhibited, although the fruits which are formed may be seedless. Fruit set may be greatly diminished at concentrations which do not decrease vegetative growth.

At still higher concentrations (about 2000 ppm) tomato plants are definitely injured, although seldom killed, by the more toxic compounds. Even at 2000 ppm, however, many of the fruit-setting chemicals cause no apparent injury. In all of these experiments the whole plant was sprayed; no effort was made to confine the spray to blossom clusters.

The effects of N-1-naphthyl phthalamic acid differ from those of other members of the series. At 0.1 ppm it causes a leaf roll, at 0.31 ppm epinasty, and at 20 ppm stem swelling (greenhouse data). In the field test it completely inhibited fruit set at 20 to 2000 ppm. The vine weight was almost normal at 20 ppm (the lowest concentration tested) but epinastic and morphological effects were severe.

N-aryl phthalimides behave much like the corresponding phthalamic acids. Compounds derived from secondary amines (formula I, where R is a hydrocarbon radical) are less active than the corresponding compounds in which R is a hydrogen atom.

Maleic Hydrazide, a Unique Growth Regulant

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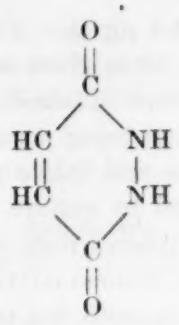
Maleic hydrazide has been found to have a pronounced, but temporary, inhibiting effect on plant growth. The length of inhibition period appears to be directly proportional to the concentration used. To our knowledge this effect is unique in that growth inhibition is obtained with little visible harm to the plants.

Maleic hydrazide, or more properly, 1,2-dihydropyridazine-3,6-dione, has the following structure (*1*):



It is slightly acidic in character and forms salts readily with alkalies. The free compound is completely water-soluble at 2000 ppm (0.2%) but does not dissolve completely at 1%. More concentrated solutions can be made using triethanolamine or other alkalies. Heavy metals precipitate insoluble salts from such solutions. Both the soluble and the insoluble salts function as growth regulants.

Maleic hydrazide, its cupric salt, and its zinc salt were dissolved or suspended in water at a concentration of 2000 ppm. Emulphor EL was used as the wetting agent at the rate of one drop per 100 mg of hydrazide. Six-inch tomato plants, variety Bonnie Best, were sprayed to run-off in duplicate with each suspension. The treated plants, in a greenhouse, failed to grow for a period of about two months. Root growth was also inhibited. The controls grew normally. After about one month some chlorosis developed on the younger leaves, but otherwise the plants were normal in appearance. After the quiescent period, growth resumed mainly from lateral buds. The plants had blossomed before they were discarded. Other tomato plants were not killed by a 1% suspension, nor did they show necrotic spots. A 1000-ppm solution produced a formative effect when regrowth started from the terminal bud. This effect was not pronounced in growth from the lateral buds.

FIG. 1. Effect of maleic hydrazide on the growth of tomato plants. Plant at right was sprayed with 2000 ppm of maleic hydrazide one month before photograph was taken. Untreated control on left shows normal growth.

TABLE 1

EFFECT OF AMMONIUM SALT OF MALEIC HYDRAZIDE ON THE GROWTH OF TOMATO PLANTS

Concentration	8 Days		14 Days	
	Ave. increase in height*	Inhibition†	Ave. increase in height*	Inhibition†
ppm	cm	%	cm	%
0	11	0	25	0
2000	2.5	77	2.5	90
1000	3.0	73	4.0	84
500	5.0	55	7.0	72

* Original height, 7 cm.

† % Inhibition = $\frac{\text{Increase in height of control} - \text{increase in height of treated plant}}{\text{Increase in height of control}} \times 100$

In another experiment, similar results were obtained using the triethanolammonium and diethanolammonium salts of maleic hydrazide. These salts seemed to be somewhat more effective than the free compound when applied at equal concentrations of the active ingredient. This increase in activity may be due in part to better wetting of the leaf surface, since we have observed that maleic hydrazide is reduced in activity when the wetting agent is omitted.

Fig. 1 shows two tomato plants one month after the one on the right was sprayed with a solution containing 2000 ppm of maleic hydrazide. During this interval the control increased in height about sixfold. It may be noted that the stem of the treated plant gave the normal increase in diameter and that leaves already formed increased normally in size. There was, however, virtually no terminal growth.

Semiquantitative growth data have been obtained on tomato plants treated in duplicate with three different concentrations of the ammonium salt of maleic hydrazide. The spray included one drop of Emulphor EL per 100 mg of the ammonium salt. Growth data were taken after 8 days and after 14 days. The results are presented above in Table 1.

Turf was treated with 8, 4, 2, and 1 lb per acre of maleic hydrazide. The chemical with Emulphor EL as the dispersing agent was applied as a spray in about 200 gal of water per acre. The 1-lb rate had a slight retarding effect; the 2-lb rate inhibited growth for 1–2 weeks; the 4-lb rate for about 4 weeks and the 8-lb rate for over 2 months, when all growth was stopped by cold weather. After the quiescent period, growth at the

1-, 2-, and 4-lb rates appeared normal. Bluegrass, bentgrass, crabgrass, plantian, and chickweed were inhibited in this experiment. Observations will be continued to determine whether the treated plants will survive the winter. During the course of this study there were several weeks without rain, and the inhibition periods might be altered in a more normal growing season.

In one experiment it took much more chemical to inhibit growth of tomato plants when the chemical was used as a soil drench than when it was used as a spray. Maleic hydrazide used as a pre-emergence treatment on a variety of different plants had no inhibiting effect when used at a rate of 8 lb per acre. When applied as a dust to corn seed before planting it had no effect on the amount or time of germination, but the seedlings suffered a marked retardation of growth. As with foliage, the amount of inhibition was directly proportional to the concentration applied.

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A Preliminary Report of the Successful Treatment of Amebiasis with Aureomycin[1]

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Amebiasis, or human infection by the protozoan parasite *Endamoeba histolytica*, is a world-wide and prevalent infection. Although a great deal of work has been done with amebicidal drugs, the treatment of this condition remains unsatisfactory. Under certain conditions, currently used amebicidal drugs, especially emetine, involve danger of toxic reactions.

In several cases of other infections treated with aureomycin hydrochloride, we observed an alteration in the gross character of the stool and a reduction in the fecal bacterial flora. This evidence of local intestinal effect, combined with its known systemic action, led us to investigate the use of aureomycin in amebiasis.

Three cases of infection with *E. histolytica* have been treated with aureomycin. While this is a small series and the patients have not yet been observed for an adequate period following therapy, we feel that the results are sufficiently encouraging to warrant a preliminary report so that investigation of this apparently useful drug in amebiasis might be furthered.

W. W., a 27-year-old white male complaining of flatulence, heartburn, diarrhea, and malaise was found to have trophozoites and cystic forms of *E. histolytica* in his stool. After the administration of 7.0 g of aureomycin by mouth in divided doses over a 3-day period, the stools became negative for *E. histolytica* and the patient became asymptomatic. At this time, the aureomycin blood level was 8 μg %. Therapy was continued until the patient had been given a total of 19 g. Six negative stools have been obtained since treatment.

No stool is reported as being negative until it has been studied by fresh saline and iodine preparations, by iron hematoxylin stains, and by culture.

B. C., a 63-year-old colored male was examined because of paraumbilical pain, abdominal fullness, and constipation. *E. histolytica*, in both the trophozoite and cystic forms, was demonstrated in the stool. After 6.75 g of oral aureomycin in divided doses over a 3-day period, the stools became negative. This patient received a total of 21.75 g of aureomycin. All of the gastrointestinal symptoms disappeared and 14 stool examinations over a period of 3 weeks have been negative for *E. histolytica*.

A. T., a 43-year-old colored female was found to have trophozoite and cystic forms of *E. histolytica* in her stools. She complained of rather severe indigestion, epigastric pain, and flatulence. In this case, the stools became negative after 15 g of aureomycin. The blood level of aureomycin at this time was 8 μg %. The patient received a total of 22.7 g of aureomycin. Seven negative stools have been observed since treatment.

In the first two cases there were no toxic reactions to aureomycin. The last patient complained of nausea for 48 hr after the initiation of treatment. No other reactions were observed.

While it was recognized that *in vitro* and *in vivo* action of antibiotics is frequently quite different, *in vitro* studies were carried out. Hewitt (*2*) demonstrated amebicidal activity of aureomycin *in vitro* on the NRS strain of *E. histolytica*. Since the NRS strain has been carried in culture for many years, we thought it might be of some interest to test *in vitro* activity of aureomycin on the three strains isolated from the above cases. Cultures were isolated and maintained in Nelson's egg yolk alcoholic extract medium (*3*). The first and second subcultures from one case, the third subculture from the second case, and the fifth subculture from the third case were used for the assay study. Inoculation of several tubes was made from each strain. These were examined at the end of 24 hr and only heavily positive cultures were used to test the activity of aureomycin. At the time of examination, aureomycin was introduced into the cultures in amounts varying from 0.2 to 3.2 mg/cc of overlay. The tubes were then examined at 6, 18, and 48 hr after the introduction of aureomycin. All ameba were destroyed at the end of 6 hr exposure in the tubes having 0.8 mg or more aureomycin per cc. Most of the ameba in tubes having 0.2 and 0.4 mg/cc were destroyed at the end of 18 hr. At the end of 48 hr no ameba were found in any of the tubes containing aureomycin, while all of the control cultures were heavily positive.

A much larger series of cases with adequate follow-up examinations after treatment will be necessary for an evaluation of aureomycin in the therapy of amebiasis. The work of Anderson, *et al.* (*1*) has shown that there is a sufficient number of cases in Memphis to allow us to accomplish this. The high blood levels obtained sug-

[1] Aureomycin furnished through the generosity of the Lederle Laboratories, Pearl River, New York.

gest that this antibiotic may be effective in extra-intestinal amebic infections such as hepatic abscess as well as in amebic colitis and amebic dysentery.

Eleven cases have since been successfully treated, with no recurrence of symptoms.

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Studies on Arthropod Cuticle. III. The Chitin of Limulus[1, 2]

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Through the years there has been sporadic discussion as to whether or not the chemical chitin is a single compound, identical in all animals and fungi. The consensus of opinion, based on the chitosan color test, nitrogen values, and X-ray diffraction diagrams, is that it is a single compound in the sense that it is always a polymer of identical acetyl glucosamine units (*1*, *3*). However, some exceptional cases have been recorded that require further investigation. The outstanding exception within the phylum Arthropoda is the cuticle of the horseshoe crab, *Limulus polyphemus*. Fränkel and Jellinek (*4*) isolated and identified glucosamine crystals from *Limulus* that were identical with similar preparations from ordinary crab shells, but their chitin preparation had a low nitrogen value (5.51% in contrast to 6.89% theoretical for acetylated glucosamine). On the basis of analyses giving a carbon-nitrogen value of 10 to 1 (in contrast to 8 to 1 for ordinary crabs) they postulated that the chitin of *Limulus* is made up of units similar to those in chitin from other arthropods, but that there is an additional ethyl or two methyl groups substituted somewhere in the units which, like the acetyl group, are hydrolyzed off during the preparation of glucosamine. To make this suggestion one has to assume that the alkali purification is reasonably complete (since chitin, having no known solvent, cannot be purified by recrystallization).

Reinvestigation of this question has led us to the conclusion that the purification procedure is at fault. Our first nitrogen analyses of alkali-purified chitin from *Limulus* were comparable to those of Fränkel and Jellinek; however, using a more complete purification process involving prolonged treatment with an oxidizing agent ($KMnO_4$ followed by $NaHSO_3$) after the treatment with hot alkali (*2*), we have obtained a pure white residue which gives a Kjeldahl nitrogen value of 6.06%. This, although significantly higher than the value recorded by Fränkel and Jellinek, is still considerably lower than the nitrogen values of chitin purified from the cuticles of other arthropods. It is suggestive of the removal of additional impurities, but is inconclusive, since chitin is not completely resistant to hot alkali. In an attempt to settle the point, we had X-ray diffraction pictures made of chitin purified from the cuticle of *Limulus* and from a local species of crayfish (*Cambarus* sp.).[3] The X-ray pictures are identical, and agree with those previously published for chitin (*2*, *3*). We are forced to conclude that the chitin units of *Limulus* are not substituted in the manner suggested by Fränkel and Jellinek and that they are almost certainly identical with those found in the cuticles of other arthropods. Probably differences do occur on the polymer chemical level (*5*, *6*), but on the constituent unit level the substance appears to be the same for all arthropods.

This finding necessitates a reconsideration of the chemical components of cuticle. As we have pointed out previously (*6*), there is no assurance that anyone has ever prepared pure chitin. Since, unlike cellulose, chitin is not known to occur in any approximation to the pure state (usually less, commonly much less, than half the dry weight of the cuticle) and since no solvent for it is known, all assumptions of purity have been based on inconclusive data. For another component to be present in the extracts studied would require only that it agree with chitin in being insoluble in and not destroyed by treatment with water, weak acid at room temperatures, hot or cold alkali at any concentration for short periods, strong oxidizing agents at room temperatures, and ordinary organic solvents, and that it be present in low enough percentage not to greatly disturb the nitrogen values. It must also be either amorphous or of nearly identical lattice spacings or else the amount present in *Limulus* chitin would be detectable in the X-ray diffraction pictures.

Accepting the idea that chitin is made of the same units in all arthropods, the discrepancies between theoretical and actual nitrogen values presumably represent unremoved components of the cuticle. If we assume that the unknown component contains no nitrogen[4] we can make preliminary estimates of the amount present based on the nitrogen determinations. Considering only some of the recent values, we have 6.6% N for lobster chitin (*2*), 6.45% N as an average figure for insect chitin with 6.28% N as the low value obtained from hardened puparia (*3*), and 6.06% N as the highest value obtained by us for *Limulus* chitin. Calculating on the basis of 6.9% N representing pure chitin, we obtain the following degrees of purity for materials studied by these authors: lobster 96%, average insect 94–95%, hard puparia 91% and *Limulus* 87% (the material used by Fränkel and Jellinek being only 80% pure).

[1] Paper No. 2447, Scientific Journal Series, Minnesota Agricultural Experiment Station, St. Paul.

[2] The work described in this paper was done under contract between the Medical Division, Chemical Corps, U. S. Army and the University of Minnesota. Under the terms of this contract the Chemical Corps neither restricts nor is responsible for the opinions or conclusions of the author.

[3] X-ray patterns made by Dr. W. N. Lipscomb, of the Chemistry Department.

[4] The unknown component cannot contain more nitrogen than chitin does, and if it contains any nitrogen then the contaminant percentage will be even higher than these calculations.

We conclude that Fränkel and Jellinek's suggestion of a substituted chitin is incorrect and that *Limulus* almost certainly contains the same chitin units as other arthropods. Accepting this, it follows that all so-called pure chitin used for analytical work contains at least several percent of an unknown contaminant, that in hardened cuticles this may be over 5%, and that in *Limulus* it is considerably more than 10%. The identity of the contaminant is at present only a matter of conjecture. It would be of considerable interest to know whether it is an as yet unrecognized compound[5] or a percentage of one of the known components that is so strongly bound to the chitin that it is not removed by the purification procedure.

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Temperature Measurement inside the Body Using a Thermistor[1]

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In recent years thermistors have been increasingly applied to the measurement of temperature in animal and man (*1, 3*). A thermistor has three important advantages over a thermocouple for measurement of temperature in the body. Due to its high temperature coefficient (−3%/° C) it is approximately ten times as sensitive as a thermocouple, assuming the same order of sensitivity of detecting device. Because of its high impedance (several thousand ohms as compared to a few ohms) lead resistances and switch contact resistances are relatively unimportant; so it is not necessary to take special pains in the wiring of associated circuits. Finally, there is no necessity for maintaining a constant reference temperature.

For these reasons it was decided to incorporate a thermistor as the sensitive element in fine catheters for measuring temperatures inside the animal body. One type of catheter for measuring the temperature inside joint spaces and muscles (*2*) consisted of a radio-opaque plastic tube 0.063 cm OD, 0.036 cm ID, varying in length from 15 cm to 1.5 meters. Catheters of larger diameter have also been made for intracardiac and intravascular observations. The thermistor was placed flush with one end, the lead wires coming out the other end.

The thermistor used for this application was Western Electric Type V597 having the following characteristics:

Diameter	0.4 mm
Temperature coefficient at 38° C	−3.1 %/° C
Dissipation constant (in still air)	0.1 mm/° C
Thermal time constant (in still air)	1 sec.

Since it was supplied with two 0.025-mm bare platinum leads 8 mm long, it was necessary both to splice these wires to a pair of copper leads, and to insulate the platinum wires and spliced junctions from each other. No. 40 enamel covered copper wire was used for the lead.

TABLE 1

Temperature Measurements in the Dog*

	°F
Superior vena cava	98.9
Coronary sinus	99.0
Right ventricle	99.0
Pulmonary artery	98.8
Inferior vena cava	98.8
Hepatic vein	98.9
Renal vein	98.4
Azygos vein	98.6
Femoral vein	96.8
Femoral artery	98.0
Thigh muscle (2 in.)	96.5
Thigh surface	92.8
Rectal	99.1

* Room temperature 73.0° F.

A connection was effected by wrapping two turns of the platinum wire tightly about the copper lead. A conducting silver paste was then applied to assure satisfactory electrical contact. In order to insulate the two platinum wires from each other, a very fine rayon thread was wrapped tightly along each wire beginning at a point on the copper wire a little below the junction. The whole assembly was then dipped into a bakelite solution, care being taken not to immerse the thermistor bead itself. After the bakelite had been baked, the whole assembly was threaded through the plastic tubing. The end containing the thermistor was then sealed with a small amount of polystyrene, care again being taken not to coat the thermistor bead which protruded a few tenths of a millimeter beyond the end of the tube.

The unit was connected into a conventional Wheatstone bridge using a Rubicon galvanometer of sensitivity 0.007 μa/mm as an indicating instrument. For recording purposes, the output of the bridge was connected to a pen-writing oscillograph. The overall accuracy of the device was ±0.05° C.

Vascular and other temperatures obtained with the thermistor units are shown in Table 1. The dog was under heavy Nembutal anesthesia. The catheter was passed through the right external jugular vein, and its position was recognized roentgenoscopically.

[1] Aided by a grant to the University of Pennsylvania from The National Foundation for Infantile Paralysis.

[5] The possibility of another type of substituted glucose chain with a side group that would give the same lattice unit dimensions as an acetylated amine group is conceivable.

Similar temperature data have been obtained in various human joints. A 19-gauge hypodermic needle was inserted into the knee joint space. The catheter was threaded through the needle and the needle withdrawn, leaving the thermistor unit in place within the joint. The knee joint temperatures of two normal adult males were found to be 90.3° and 91.2° F respectively, while the surface or skin temperatures were 84° F.

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A Comparative Study of Oyster Condition[1]

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The necessity of providing an objective evaluation of the condition of oysters in ecological investigations has long been recognized by workers in this field. The condition index originally proposed by Hopkins (*1*), which depends upon the measurement of the ratio of dry meat weight to internal shell volume has not been entirely satisfactory for this purpose. Many workers have found considerable variation in this index among oysters from the same region, even where the condition of meat by visual comparison appeared to be relatively constant.

For this reason later workers have adopted the measurement of glycogen content as a supplementary method of evaluation (*2–4*). Since this method appears to yield more consistent results, a study was carried out to determine correlation between condition index and glycogen content.

In all, 30 samples of oysters from various habitats of the Louisiana oyster bayous and four samples from the outside tanks of the U. S. Fisheries Station, Pensacola, Florida, were taken, and each sample was analyzed by both methods.

In arriving at condition index a 10-g aliquot of the ground oyster tissue from 10 oysters was dried at 80° C for 48 hr and weighed. After 15 min in the air it was again dried and weighed to constant weight ±.005 g. The dried weight of the 10 oysters was then calculated and entered into the formula:

$$\frac{\text{Total dry weight in g} \times 100}{\text{Shell cavity volume}} = \text{Index of condition.}$$

Shell cavity volume was obtained by water displacement.

Five to 10 g of the same sample of ground oyster meats was digested and the glycogen was hydrolyzed by the Calderwood-Armstrong method (*5*). The Hagendorn-Jensen technique (*6*) for the quantitative determination of glucose followed. To insure against enzymatic action, not more than 3 min was permitted to elapse between grinding the meats in a Waring blender and the digestion of the aliquot in sodium hydroxide.

Fig. 1 shows the correlation between the findings of the two methods. Closer correlation appears to exist among animals of the higher glycogen content and presumably greater vigor. In fact, the correlation coefficient of .69 for the entire group is reduced to .38 if the three samples highest in glycogen are omitted.

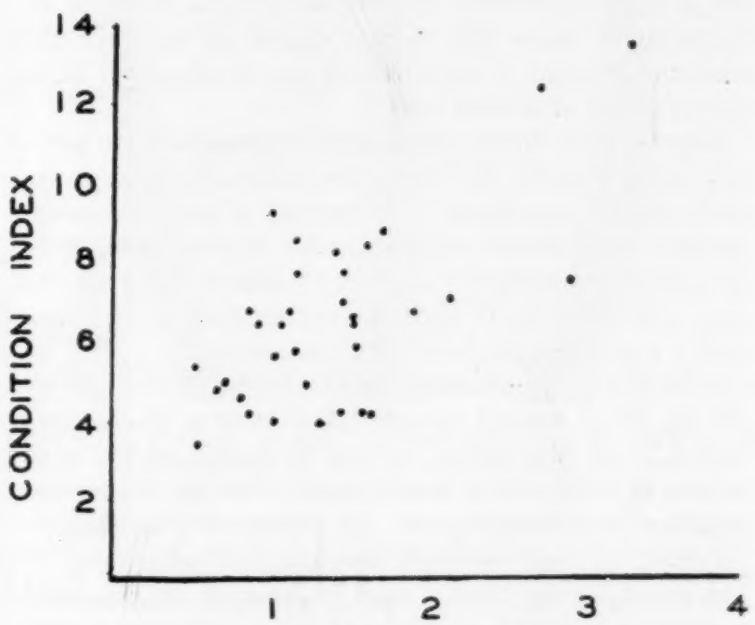

FIG. 1.

It is concluded from these preliminary studies that the poor correlation between the two methods in oysters of low vigor is probably due to dependence of the condition index upon water content, absolute size of meats, and other factors. Because of this, it is believed that glycogen analysis is the most suitable method for the comparison of work carried out by independent investigators on low quality oysters. Further work is under way to determine if a significant correlation exists between the two methods in high quality oysters.

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[1] Facilities and support for this investigation were supplied by the Department of Wildlife and Fisheries of the State of Louisiana.

[2] The author is indebted to Drs. F. G. Walton Smith and H. Malcolm Owen for advice and to Louis A. Bregan, Jr., for technical assistance.

Maximal Consumption of Ethyl Alcohol

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Physicians who have had to deal with patients suffering from chronic alcoholism cannot but have been impressed with the wide variation in estimates given by them when asked how much they drink daily. In general, they fall into one of two classes: those who state that they never take more than a couple of beers, and those who stoutly maintain that they consume up to 2 qt of whisky every 24 hr. In order to have some basis for judging the credibility of these statements, it would be desirable to know with a fair degree of accuracy the maximum amount of alcohol that can be consumed daily over a period of several days.

Simple as the direct experimental approach to the problem would seem to be, the medical literature fails to record such an experiment. In default of such direct appraisal, which should certainly some day be made, there is available a sufficient amount of data bearing on the subject to allow us to estimate the maximal daily intake with a reasonable probability of accuracy.

Widmark (*7*) estimated, on the basis of the rate of fall of blood alcohol concentration after a single dose, that a 70-kg man should be able to dispose of 170 g of alcohol in 24 hr, which would imply a rate of alcohol metabolism of 101 mg/kg/hr. If Widmark's estimate is accurate, we must conclude that the greatest amount of 100 proof whisky that a man of average weight could metabolize in a day would be 14 oz, or less than a pint, which would certainly render inaccurate the estimates frequently given of a consumption several times this great. Nor can it be argued that the greater capacity claimed by addicts may be due to increased facility in alcohol metabolism engendered by habituation, for this has been found not to be the case (*3*).

Before we prematurely discredit the patients' statements, however, we must consider an important factor which probably operated to make Widmark's estimate too low. This is the finding, recently confirmed (*1, 4*), that the rate of alcohol metabolism is not constant irrespective of dosage, as Widmark believed, but that it increases with increasing blood alcohol concentration. Thus Eggleton (*1*) found by referring back to Mellanby's original work (*2*) that in the dog, when the blood alcohol concentration was between 300 and 400 mg/100 cc, the rate of alcohol metabolism was 200 mg/kg/hr; whereas when the concentration was between 200 and 300 mg/100 cc, the rate was only 150 mg/kg/hr. Similarly Newman and Lehman (*5*) found that, considering the average for four dogs, an increase in dosage of 100%, which would double the average blood alcohol concentration, produced an increase in rate of alcohol metabolism of 36%. This has since been confirmed by Newman, Yee, and Cutting (*6*). Since most of Widmark's work was done with small doses of alcohol, the increase in rate of metabolism with increasing dosage may well be responsible for the low estimate of maximal daily consumption reported by this generally reliable worker.

That maximal daily consumption is indeed higher than that put forward by Widmark is supported by the amount of alcohol that has been consumed day after day by dogs in this laboratory. Thus three dogs were allowed access at all times to a solution of 5% by volume of ethyl alcohol in tap water as their sole source of fluid. Under these circumstances they consumed alcohol at a rate of 4.46 g/kg/day. When the percentage of alcohol was raised to 10% they reduced their fluid intake accordingly, so that their alcohol intake increased only to 5.52 g/kg/day. This is equivalent to 230 mg/kg/hr, which is quite a close approximation to the 200 mg/kg/hr that was found by Mellanby with high alcohol dosage. If we transpose this to man, the maximal daily dosage for a 70-kg man can be calculated to be 386 g of alcohol, or approximately 32 oz of 100 proof whisky. This is much nearer the intake claimed by many alcoholics.

A reasonable criticism of the above inference is that so far no evidence has been put forward to justify equating the rate of alcohol metabolism in dog and man. There is, however, fairly conclusive evidence that such an equation is tenable. Thus Newman and Lehman (*5*) found as the average for two human subjects after a dose of 1.5 g/kg, a rate of metabolism equal to 214 mg of alcohol/kg/hr, quite comparable to the figures for dogs which we have quoted. Thus it seems quite reasonable to assume that the rate of metabolism of alcohol in man and in the dog is essentially the same.

Further evidence regarding the rate at which alcohol can be metabolized in dogs may be secured from the following experiments. A 23-kg male dog was given a dose of 3.0 g of alcohol intravenously, and the blood alcohol concentration followed until it approached zero. The average rate of metabolism of alcohol so determined was found to be 156 mg/kg/hr. On another day the same dose was again given, followed by a constant intravenous infusion at a rate of 156 mg/kg/hr for a period of 3 hr. The blood alcohol concentration under these circumstances dropped from an initial figure of 363 mg/100 cc at the start of the constant infusion to 351 at the end. On two other occasions an initial dose of the same magnitude was given, followed by hourly doses administered by stomach tube at the same rate of 156 mg/kg/hr for a period of 8 hr. On one occasion the blood alcohol concentration dropped from 346 to 312 mg/100 cc, on the other from 330 to 312. Thus, in spite of the maintenance dose of 156 mg/kg/hr, calculated from the average rate of disappearance of alcohol after a single large dose, there was, on the average, a drop in blood alcohol concentration of 3.5 mg/100 cc/hr, which is equal to a rate of metabolism of 30 mg/kg/hr in excess of the maintenance dose. The experiment thus demonstrated that a maintenance dose of alcohol calculated from the average rate of metabolism after a single large dose was not sufficient to maintain the blood alcohol level constant at the highest level produced by such a dose. This constitutes additional proof of the fallacy of the hypothesis that the rate of alcohol metabolism is unrelated to dosage or blood

alcohol concentration. The true rate of alcohol metabolism at this high blood alcohol concentration can thus be estimated as the sum of the maintenance dose of 156 mg/kg/hr plus the deficit of 30 mg/kg/hr, or 186 mg/kg/hr. If this rate be applied directly to man, the maximal daily consumption for a 70-kg man would be 312.5 g of alcohol, or about 26½ oz of 100 proof whisky, which falls in the same order of magnitude as the 32 oz calculated from prolonged daily consumption in dogs.

From these data we may then conclude that the maximum daily consumption of alcohol by a man of average weight is represented by a quart of 100 proof liquor, and that estimates greater than this are in error. Equally, it may be concluded that this consumption may only be achieved by maintaining the blood alcohol concentration at a high level.

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Preliminary Observations on the Biological Effects of Radiation on the Life Cycle of *Trichinella spiralis*

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Trichinella spiralis is the causative agent of human trichinosis. The disease is acquired as a result of eating undercooked meat, usually pork, containing the parasite in the encysted larval stage. Trichina infection appears to be somewhat common in the United States as it has been found in 14.34% of human post-mortem examinations (*2*). Since there is no simple economical method of treating meat at slaughter to kill trichinae larvae, any information which may improve present conditions is desirable. It has been found that a very intense beam of X-rays or cathode rays produced in a newly developed high voltage machine rapidly destroyed bacteria, yeasts, and molds, and the application of this method to the sterilization of food has been suggested (*1, 3*).

The writers, in this study, have undertaken some preliminary experiments to determine whether treatment of meat with radiations would have lethal action on the encysted trichinae larvae or would produce some morphological change which would prove detrimental to the life cycle of the parasite. For the purpose of clarity the life cycle of *Trichinella spiralis* is briefly summarized. The larvae develop and reach maturity in the intestinal tract of the host 2–3 days following ingestion of infected meat. On the fifth or sixth day about 99 to 100% of the female worms show embryos in the uterus (Fig. 1a). These embryos are liberated into the lymph spaces of the host's intestines and eventually reach the musculature where they become infective in less than 3 weeks.

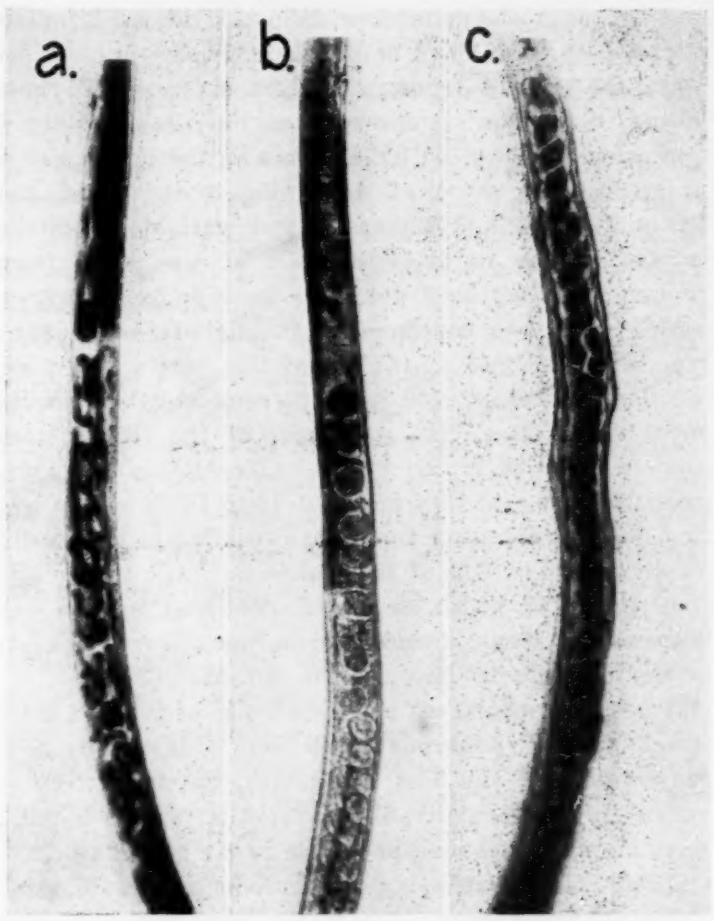

FIG. 1. Adult females of *Trichinella spiralis* recovered from small intestine of rats 6 days following experimental infection. (a) Normal adult with embryos in the uterus, recovered from a control rat which had received nonirradiated infected muscle; (b) adult showing undeveloped embryos in the uterus recovered from a rat which had received infected meat irradiated for 96 hr; (c) adult recovered from a rat which had received meat irradiated for 144 hr showing abnormality in the shape of the body wall.

The method used in these experiments consisted in preparing small cellophane wrappings each enclosing about 1 g of trichinous rat meat and placing the packets between two tubes containing radioactive cobalt, in a refrigerator at about 4° C. The dose of irradiation received by the meat was estimated to be 2000 r for each 24 hr, consisting largely of gamma rays, the beta rays having been filtered out. After the meat was irradiated for a specified interval of time, the contents of each of two wrappings were fed to each of two white rats.[1] One of the rats was killed 6 days after infection to determine the condition of the adult worms in the intestinal tract. The second rat was killed 30 days after infection to determine presence or absence of encysted trichinae larvae in the musculature; if larvae were not found by use of the press preparation method, the muscle was artificially digested and examined. A control rat receiving un-

[1] Acknowledgment is made to Dr. A. R. Lamb, Experiment Station, H.S.P.A., for making laboratory animals available.

treated meat was maintained for each rat fed irradiated meat; both were killed at the same time.

In the present report, based on six separate experiments, the following observations have been made: Irradiation produced no lethal effect on the larvae nor did it affect their power of developing to the adult stage. Irradiation showed increased and variable deleterious effects on the reproductive cells of the adult female worms with increased dosage. In four experiments in which meat was continuously irradiated for 4 days it was estimated that 12 to 86% of the female worms were sterile, i.e., the embryos failed to complete their development (Fig. 1b). The remainder of the female worms showed embryos in the uterus. Irradiation for 5 days resulted in the sterility of about 43 to 100% of the adult females. Irradiation for 6 days resulted in the sterility of about 60 to 100% of the female worms. In two other experiments in which meat was irradiated for 4–6 days, presence of sterile female worms was observed but the percentage affected was not determined.

Female parasites, not made sterile as a result of irradiation, produced embryos which were able to invade the musculature of the host and become infective. Of six rats receiving meat irradiated for 6 days, and killed 30 days later, four showed no larvae in the musculature.

In addition to affecting the reproductive tissue, irradiation produced abnormality in the form of irregular elevations or vesiculations of the body wall of the parasite (Fig. 1c). This condition was evident along the posterior half of the female worm and was found to be more prevalent as the period of irradiation increased.

These results show that gamma radiation at the dose, intensity, and temperature applied is not lethal to trichinae larvae encysted in meat, but under proper dosage renders the female worms sterile and unable to complete their life cycle. Experiments are in progress to determine, among other things, the effects of larger dosages applied for a shorter time from a more intense source.

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Effect of Temperature on the Mutual Adhesiveness of Epithelial Cells[1]

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Previous work in our laboratory has demonstrated that an important physical characteristic of cancer cells is decreased mutual adhesiveness, and that this property is apparently due to a low calcium content of such cells (*1*, *3*, *4*). These observations have stimulated investigation of other factors which might affect normal cell adhesiveness and have led to the finding that adhesiveness is greatly affected by temperature.

[1] Aided by a grant from the Donner Foundation.

The method used has been described previously (*1*), and only a summary will be given here. Attached pairs of human buccal epithelial cells were used. The force required to separate each pair by micromanipulation was measured. This force, calculated in milligrams, was determined by measuring the bend produced in a previously calibrated microneedle as it was moved in a direction tending to separate one member of a pair of cells from the other. During micromanipulation, the cells were kept immersed in a balanced salt solution. A constant high temperature was maintained by a warm box surrounding the micromanipulator; and a low temperature, by the use of a refrigerated room.

Adhesiveness of the epithelial cells was determined at three different temperatures. At room temperature of $22.5 \pm 1°$ C the mean force required to separate 100 pairs of cells was 1.53 mg, with a standard error of ± 0.067. When the epithelial cells were separated at $37 \pm 1°$ C, their adhesiveness was found to have decreased; the mean value for 50 pairs of cells was now 0.88 mg, with a standard error of ± 0.070. This value was significantly lower than that obtained at room temperature, for the difference in means was 6.7 times the standard error of their difference. Thus, it is concluded, an increase in temperature produced a decrease in adhesiveness of buccal epithelial cells.

When epithelial cells were separated at a low temperature ($11 \pm 1°$ C), the mean value of adhesiveness for 100 pairs of cells was 1.91 mg, with a standard error of ± 0.100. This value was significantly higher than the room temperature value (1.53 mg), as the difference in means was 3.16 times the standard error of the difference. It is concluded, therefore, that a decrease in temperature produced an increase in adhesiveness of epithelial cells.

These results demonstrate that changes in temperature can significantly alter the adhesiveness of cells to each other. While quantitative measurements of most biological and biochemical processes change in the same direction as does the environmental temperature, the property of adhesiveness changes inversely as the temperature. Alterations in adhesiveness produced by changes in temperature may be of no great significance in homoiothermic animals, where body temperature remains approximately constant. However, such alterations are probably of importance in cold-blooded animals. Thus, Lucké and Schlumberger (*2*) have demonstrated that renal carcinoma of the leopard frog metastasizes more extensively when the environmental temperature is increased. Conceivably, increase in temperature may further reduce the already decreased adhesiveness of cancer cells, thereby leading to greater invasiveness and enhancing the chances for vascular dissemination.

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Comments and Communications

The Electrochemical Restoration of Badly Corroded Silver-Copper Alloy Objects

The ancient Egyptians and the peoples that followed were well acquainted with the hardening effect of copper upon silver (sterling silver contains from 7.5% to 10% copper). Accordingly, it is not uncommon to come upon so-called "silver articles" during explorations and excavations of historical sites in Egypt or other countries bordering on the Mediterranean Sea.

The objects we investigated were found in graves or buried in the soils of Egypt, Greece, and elsewhere. The objects when found presented the appearance of badly corroded bronze objects with no indication that they were silver alloys. Accordingly, the objects were classified as copper-tin "bronze." They had the usual green-gray crust of corrosion products comprising the basic carbonates of copper, malachite, and azurite, together with a substructure of red cuprite. Intimately mixed with these copper compounds was a porous mass of clay or sand.

Accordingly, we treated the objects by our standard method for bronzes, making the objects cathode in a 2% solution of sodium hydroxide. It was not until the copper compounds had been reduced to metal that we met with the first indication that silver was present in this or that object. This silver was in the metallic state and located underneath the reduced copper. On the basis of the restoration results of a number of copper-silver objects we have enough evidence to indicate that the silver copper alloys were selectively corroded, copper going into solution in the acid or salt solutions found in soils. As long as any metallic copper was present this would protect the silver by causing it to become cathodic. Accordingly, we find the silver metal imbedded in a mass of copper compounds.

The corrosion of silver does not take place until all of the accessible neighboring copper has been oxidized. Corrosion proceeds radially from the original surface, and at a certain distance away from the original phantom surface the silver is precipitated, forming a structure that is frail but that reveals, somewhat magnified, the details of design of the original object. After the copper metal has been eliminated the silver is attacked by soil acids or soil salts in solution in the moisture in the soil: the reduction of the several silver compounds, notably the chloride and the black oxide, proceeds without much difficulty.

In a number of cases we have observed that the silver coin was larger in total volume than the original coin. The same observation applies to other silver objects. It would seem, therefore, that in the corrosion of a silver-copper coin there are a number of more or less distinct steps or stages:

1. The attack of the copper constituent by the corroding liquid in the soil.

2. The migration of the copper compounds, such as chlorides and sulfates into the porous or veined loamy soil. Eventually these copper compounds migrate until they reach the air and are then converted into basic salts such as malachite.

3. The dissolution of the copper constituent of the coin or other "hard silver" object continues through many years until only the silver remains.

4. During this process of copper dissolution, the silver constituent is electrochemically protected as long as metallic copper is present.

5. As soon as the copper is all corroded its protective action on silver stops, and the corroding agents attack the silver.

6. Silver salts migrate through the soil and pass copper salts until they encounter organic plant and animal matter. This matter has a strong reducing action on the silver salts and after considerable time has elapsed, a somewhat enlarged pure silver replica of the original "hard silver" object is formed.

7. These replicas are isolated during the process of restoration. The reduction of silver compounds to silver metal may not take place in the soil but it will take place during the electrolytic process of restoration.

COLIN G. FINK

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A Third Record of the Whale Shark, *Rhineodon Typus,* in the Caribbean Sea

In 1935, I published an article on the geographical distribution of the whale shark in which all known specimens were located. Because of its occurrence in the Gulf of Mexico, off Havana, Cuba, in the Florida Keys, and off the East Coast of Florida, I had long felt sure that Rhineodon must be found in the Caribbean Sea. In 1926 and in 1934, second- and third-hand reports came in that a great shark (thought to be Rhineodon) had been seen off Trinidad in the Gulf of Paria, and that another had been repeatedly observed off San Juan Harbor, Puerto Rico. Every effort was made to get definite data for each shark, but in the end these fish had to be put down as unverified possibilities of whale sharks.

First Record. Better fortune came later. On April 26, 1934, the *New York Herald-Tribune* recorded a great shark rammed and killed by the Grace liner *Santa Lucia,* on the run from Cristobal (Colon, Canal Zone) to Cartagena, Colombia. Correspondence with the Grace Line officials resulted in a visit to my office by Chief Officer A. E. Richards, who gave an exact description of the great fish. Here, then, was the first definite record of the occurrence of the whale shark in the Caribbean. This observation I published in 1937.

Second Record. Further definite evidence that Rhineodon occurs in the Caribbean came in 1937. The curious behavior of a great shark in the harbor of St. Marc, Haiti, around the steamer *Colombia* of the Colombian Steamship Company, was noted in a newspaper clipping sent me. A letter to the office of the company brought an answer from Pres. C. H. C. Pearsall, who at the time was on the steamer in the harbor of St. Marc. His description of this great fish positively identified it as Rhineodon, and this was verified by his inspection of a photograph in my office.

Mr. Pearsall carefully described the unusual behavior of this greatest of the sharks. It "hung around" the steamer while she was loading bananas under a strong electric light. A number of shots were fired at the unwelcome visitor, but they glanced harmlessly from his body armor of denticle-covered 4-inch skin. Once Rhineodon came up under the companionway, raised its head and dislodged the platform at the bottom of the ladder. The shark was about 25 feet long and when it bumped into the side of the ship, the impact was noticeable. An account of this fish and its behavior appeared in 1939.

Third Record. And now comes another authentic account of a whale shark in the Caribbean. Mr. Arlo Kalsheim, second officer of the tanker *Marathon* of Oslo, Norway, has kindly sent me a letter, via the U. S. Hydrographic Office, Washington, D. C., giving the following data. The *Marathon*, on a passage from Lisbon, Portugal, to Puerto La Cruz, Venezuela, had arrived on January 14, 1949, and anchored in that harbor in the afternoon. The officers were on the bridge awaiting orders from shore, when the captain called attention to a huge shark swimming near the vessel. Mr. Kalsheim writes that it was about 30 feet long and was swimming toward the ship. He had seen my article and figure published in the Hydrographic Bulletin in 1934 and at once recognized the visitor as a whale shark. He wrote that it was covered with spots over its whole body, as the published figure showed, and he estimated the width of the huge mouth at 4 feet. The great shark swam about the ship until dark, feeding on swarms of small fish and on other organisms at the surface. None of the ship's company had ever seen a shark of this size, shape, and color. It stayed on the shady side of the ship and hence it was impossible to take a photograph.

This behavior of the third Caribbean whale shark parallels that of the second specimen noted in these waters and of the two others which were reported by hearsay that could not be verified. This third Rhineodon had no fear of the ship or the crew, who, to a man, were hanging over the rail keenly interested. This behavior is typical of the whale shark. Secure in its armor of 4-inch-thick hide of tough fibers, the adult can be harmed by nothing that swims the seas. It has no enemies but man, and his harpoons and bullets will not penetrate its skin save when this is relaxed and shots are on the perpendicular—at an angle they glance off harmlessly. Man's surest way of killing this sluggish monster is by ramming it with a steamship—and a considerable number of such cases have been reported by the present writer (1940).

Those interested in the habits and behavior of *Rhineodon typus* will find all available material presented in my article, "The Whale Shark Unafraid," published in 1941.

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Some Current Misconceptions of N. L. Sadi Carnot's Memoir and Cycle

Recent authoritative texts state erroneously that Carnot (1824): (a) employed the discredited substantive or so-called caloric theory of heat, (b) discovered the second law without appreciating the first law, and (c) incorrectly pictured the descent of heat (*chute de calorique*) through an engine as analogous to the flow of water through a mill.

These misconceptions have arisen from improper interpretations of Carnot's terms *feu* (flame), *chaleur* (heat), and *calorique* (translated as "caloric" but should be interpreted today as entropy following Brønsted).

Clapeyron (1834) misunderstood Carnot and introduced unnecessary mistakes which Carnot had been careful to avoid. (CALLENDAR, H. L. "Heat" in *Encycl. Brit.*, 1911, *et seq.*). Clapeyron's mistake still dominates the literature a century later.

Kelvin (1849–51) interpreted the three terms indiscriminately as heat and unjustly criticized Carnot's proof. Clausius (1850) was acquainted with the memoir only through the work of Clapeyron and Kelvin. Ostwald (1892, *Klassiker* No. 37) remarked that Carnot used *chute de calorique* consistently when emphasizing the motive power of heat, but *chaleur* for general consideration, never *chute de chaleur*.

Brønsted (1937–47, *Phil. Mag.*, 1940, **7**, 29: 699), has developed a new self-consistent and symmetrical system of energetics in which the reversible transport of any extensive quantity (entropy, mass, electric charge, etc.) through a corresponding conjugate difference in potential (temperature, gravitational or electric, etc.) is necessary for the production of work. (LA MER, FOSS and REISS, *Conference on molecular interaction*, New York Academy of Sciences, Am. N. Y. Acad. Sci., 1949, 51, Art. 4).

Carnot's cycle thus represents the conversion of thermal energy (TS) into mechanical work A by the fall of entropy through a potential difference ($T_2 - T_1$)

$$\delta A_{\text{thermal}} = \delta S(T_2 - T_1)$$

Brønsted's interpretation simplifies the presentation and renders unnecessary the accepted compensation theory of Clausius developed to harmonize Carnot's ideas (as Clausius understood them) with the first law.

This communication is based on a paper presented at the January 29 meeting of the American Physical Society. A fuller account documenting the assertions will be submitted to the *American Journal of Physics*.

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NEWS and Notes

Eduardo De Robertis, U. S. Public Health special fellow at the Department of Biology, Massachusetts Institute of Technology, has been appointed director of the Department of Cell Ultrastructure at the Institute of Biological Sciences, Montevideo, Uruguay.

Charles P. Huttrer, senior research chemist at the Warner Institute for Therapeutic Research, New York City, has been appointed research associate to the Subcommittee of Chemotherapy at the Chemical-Biological Coordination Center of the National Research Council.

Francis Birch, professor of geology at Harvard University, has been named Sturgis-Hooper Professor of Geology. He succeeds **Louis C. Graton,** who will retire this summer to become professor emeritus.

Ray C. Anderson, formerly a medical geneticist of the Army Medical Corps stationed in Hiroshima, has been named assistant director of the Dight Institute of Human Genetics at the University of Minnesota.

Charles L. Shrewsbury, of Midwest Research Institute, has been named chairman of agricultural chemistry at Southwest Research Institute of San Antonio and Houston, Texas, and associate director of the affiliated Foundation of Applied Research.

Visitors to U. S.

Hans Weddington, Fritz Wilhelm, and **Gerhard Bantzer,** German economists, are visiting a number of U. S. land grant colleges to study methods of distributing current economic information to German farmers.

Roberto Jaset, director of the Mineração Geral do Brasil, and of Usina Santa Olimpia Indústria do Ferro e Aço of South America, is studying different types of industrial equipment in this country. He plans to be here for three months.

B. L. Van der Waerden, of the University of Amsterdam, will be visiting professor for the summer quarter at the University of Washington, where he will give courses in algebraic geometry and operational methods in mathematical physics.

Grants and Awards

The Rockefeller Foundation has awarded to Duke University a grant of one hundred thousand dollars toward researches in physical biochemistry of proteins at the School of Medicine, under the direction of Hans Neurath. The grant is available for a seven-year period, beginning July 1, and has been made in addition to a similar grant of twenty-five thousand dollars awarded in 1946 for a five-year period.

Research Corporation has announced recent grants totaling nearly $250,000 to aid scientific research in colleges, universities, and institutes. One of the 65 grants—$54,550—went to George W. Kidder of Amherst College, for continuation of his work in cancer research, and another to Edward C. Kendall, of Mayo Clinic, for further study on the control of rheumatoid arthritis by an adrenal hormone.

The **John Wesley Hyatt gold medal** and $1,000 award were presented to George T. Felbeck, vice president, Carbide and Carbon Chemicals Corporation, New York City, at the annual meeting of the Society of the Plastics Industry. Dr. Felbeck received the award for engineering developments leading to the manufacture of polyethylene resins and plastics.

Mark Nickerson, assistant professor of pharmacology, University of Utah College of Medicine, was awarded the 1949 **John J. Abel Pharmacology Prize**—a bronze medal and $1,000—for his research on the pharmacology of the β-haloalkylamines, a new class of adrenergic blocking agents. The award, donated by the Eli Lilly Company of Indianapolis, will be made again in 1950. Inquiries may be addressed to the Secretary of the Society for Pharmacology and Experimental Therapeutics, H. B. Haag, Medical College of Virginia, Richmond 9, Virginia.

Sigma Delta Epsilon, the graduate women's scientific fraternity, is offering an award of $500 for research in the mathematical, physical, or biological sciences. The award, open to members only, will be made for an original research paper which has been published or accepted for publication this year by a scientific journal. Members of the research award committee are: Lela V. Barton, Boyce Thompson Institute for Plant Research, Inc., chairman; Elva Shipley Meyer, University of Wisconsin zoologist; and Helen Oldham, Department of Home Economics, University of Chicago. The award will be presented at the December meeting of the AAAS in New York City.

John Reenstierna, professor emeritus of Upsala University, Sweden, has been awarded the Finlay Order, Cuba's highest distinction, in recognition of his research leading to the development of a successful lepra serum.

This year's $2,000 **Charles L. Mayer "Nature of Light"** Prize has been awarded to Julian S. Schwinger, professor of physics at Harvard University. Dr. Schwinger won the award for his essays "On Quantum-Electrodynamics and the Magnetic Moment of the Electron."

Fellowships

The American Association of University Women has awarded 27 research fellowships of $1,500 each to women scholars for the coming academic year. Ten women scientists included among the recipients and their subjects of investigation are: Charlene Craft, instructor of anthropology at the University of Alaska, who will conduct an archaeological field trip into Upper Kuskokwim, the homeland of the Athabaskan Indians; Barbara D. Blanchard, assistant professor of zoology at Santa Barbara College, University of California, who will study the birds which migrate between California and

Alaska to learn the physiological effects of Arctic conditions on warm-blooded animals; Jacqueline Chittenden, lecturer in classical archaeology at the University of Edinburgh, who will do research on archaeological monuments relating to the cult of Hermes at the American School of Archaeology in Greece; Geneva Sayre, professor of biology at Russell Sage College, who will write a monograph on the varieties of rock-growing mosses of the *Grimmiaceae* family; Adela Cabezas, resident physician at Hospital Rosales, San Salvador, who will come to this country for postgraduate study in pediatrics; Alice B. Dickinson, fellow at the University of Michigan, who will do research in higher mathematics; Helen R. Garman, research assistant in plant physiology at the University of Wisconsin, who will study organ formation in plants; June Zimmerman, Physical Chemistry Laboratory, Oxford, who will complete a study of oxidation in bacterial systems; Lydia Bidinost, Buenos Aires biochemist, who will conduct advanced research in biochemistry at Columbia University; and V. Oldfelt, pediatrician, of Stockholm, Sweden, who will study virus diseases at Children's Hospital in Philadelphia.

Colleges and Universities

Construction of the $2,075,000 Nathan Goldblatt Memorial Hospital at the **University of Chicago** began officially with the laying of the cornerstone on May 17. To be completed in 1950, it will be the first unit in the university's $8,500,000 cancer research center. Adjacent to the Goldblatt unit, the Atomic Energy Commission will build the Argonne Cancer Research Hospital, for research on radioactive isotopes in cancer treatment.

The Massachusetts Institute of Technology has announced that Pomona College of California and Wesleyan University of Connecticut are the most recent additions to the cooperative liberal arts and technological study program which was established in 1936. The program offers qualified undergraduate students a specially planned three-year course in any of the 14 participating liberal arts colleges and enables them to complete in two years the requirements for a science, engineering, or city planning degree at M.I.T. Both a B.S. degree from M.I.T. and a B.A. degree from the liberal arts college are awarded on completion of the program. The other 12 participating colleges are: Amherst College, Amherst, Massachusetts; Bowdoin College, Brunswick, Maine; Miami University, Oxford, Ohio; Middlebury College, Middlebury, Vermont; Ohio Wesleyan University, Delaware, Ohio; Reed College, Portland, Oregon; Ripon College, Ripon, Wisconsin; St. Lawrence University, Canton, New York; Washington and Jefferson College, Washington, Pennsylvania; College of William and Mary, Williamsburg, Virginia; Williams College, Williamstown, Massachusetts; and College of Wooster, Wooster, Ohio.

The Department of Engineering Physics at Cornell University will offer a course in electron microscopy next fall, as a project of the new Electron Microscopy Laboratory, which will be established at the university as the result of a grant from the Rockefeller Foundation.

The Armour Research Foundation of Illinois Institute of Technology has begun research to stabilize calcium oxide (lime) for use as a refractory for rocket liners, jet airplane parts, and other industrial applications. The stabilization process, which will be directed by J. Scott Griffith, supervisor of ceramics, and John Neff, head of minerals research, is the second step in the project which the foundation is conducting for the Air Materiel Command. It must be preceded by the modification of high temperature electric furnaces so that they can be used up to 2300° C for sintering lime and other common oxides such as magnesium oxide.

Purdue University has established a permanent natural area of 70 acres, 12 miles from the campus, to preserve the biota for ecological study by the Department of Biological Sciences. This tract was bequeathed to the university by the late David E. Ross and is to be known as the Ross Biological Reserve. The land borders the Wabash River, and includes oak-hickory forest, bottomland forest along the river, two ravines with permanent streams, swampland, and old fields of several successional stages.

Industrial Laboratories

Mallinckrodt Chemical Works has elected as its new president Joseph Fistere, former vice president and director of the company. Mr. Fistere succeeds the late Arthur C. Boylston, who had been president since 1941.

Airborne Instruments Laboratory, Mineola, New York, has recently organized a research group known as the Applied Physics Section, headed by Rodney F. Simons. The new unit is developing a neutron velocity selector for Brookhaven National Laboratories, to be ready for use when the new atomic pile begins operation.

Meetings and Elections

An international conference on science abstracting will be held at Unesco House, Paris, June 20–25 for the purpose of developing and improving abstracting services for the natural sciences—both pure and applied—and considering methods of increasing their usefulness to scientists. Representatives from the member states of the United Nations and from its specialized agencies and other international organizations have been invited to take part in the conference. Others will be welcome as observers.

An international conference on electron microscopy will be held at Delft, July 4–7 under the auspices of the Section on Applied Physics of the Netherlands Physical Society. The meetings will include sections on Image Formation and Contrast, Resolving Power and Apparatus, and Specimen Techniques. American members of the Recommendation Committee are: Francis O. Schmidt, president, Electron Microscope Society of America; Charles J. Burton, secretary of the society; and Ralph W. G. Wijckoff, of the Department

of Microbiology, National Institutes of Health, Bethesda, Maryland. Scientists interested in participating should write to Henri Polak, Technical Documentation and Information Center for the Netherlands, 525 Rolling Road, Chevy Chase 15, Maryland.

The American Association of Blood Banks will hold its second annual meeting in Seattle, Washington, November 3–5. The program is expected to interest both scientists and administrators of blood banks and hospitals. Further information may be obtained from the Office of the Secretary, 3301 Junius Street, Dallas 1, Texas.

The Kansas Academy of Science, at its 81st annual meeting at Kansas State College on April 28–30, elected the following officers: president, Paul G. Murphy; president-elect, A. B. Leonard; secretary, A. M. Guhl; treasurer, Standlee Dalton; and librarian, D. J. Ameel.

L. A. Maynard, professor of nutrition and biochemistry of Cornell University, and Rene J. Dubos, bacteriologist and member of the Rockefeller Institute for Medical Research, have been elected trustees of **Science Service.** Dr. Maynard was nominated by the National Academy of Sciences and Dr. Dubos by the National Research Council.

The following officers were renamed at the annual meeting: president, Harlow Shapley, director of Harvard College Observatory; vice president and chairman of the Executive Committee, Alexander Wetmore, secretary of Smithsonian Institution; treasurer, O. W. Riegel, director of Lee School of Journalism, Washington and Lee University; secretary, Watson Davis, director of Science Service. Additional members elected to the Executive Committee were: Frank R. Ford, editor, *Evansville Press*, Evansville, Indiana, and Karl Lark-Horovitz, Purdue University.

Deaths

Paul Bell Davis, 60, research chemist, died March 19 at his home in Baltimore. Dr. Davis, a member of the research and development branch of the Davison Chemical Company of Baltimore since 1919, was best known for his work in silicic acid gels during World War I.

Paul Harkai Schiller, 40, died in a skiing accident on Mt. Washington, New Hampshire, on May 1. Dr. Schiller, formerly head of the Psychology Departments at Pazmany University, Hungary, and Bolyai University, Rumania, had been research associate at the Yerkes Laboratories of Primate Biology in Orange Park, Florida, since 1947. At the time of his death he was temporarily engaged in research in the Department of Psychology at Harvard University.

Arthur Berkeley Yates, 48, chief geologist of the International Nickel Company, died May 10 in Montreal, where he had gone to receive the Barlow Memorial Medal of the Canadian Institute of Mining and Metallurgy at the institute's annual convention. He had been stationed in South Africa by International Nickel.

George T. W. Patrick, 92, professor emeritus of philosophy at Iowa State College, died of a heart attack at his home in Palo Alto on May 21. Professor Patrick's fields of investigation included the psychology of social reconstruction and the philosophy of the mind.

A Directory of Translators has been established by the Science-Technology Group of Special Libraries Association. It is located at the Southwestern Research Institute, San Antonio, Texas, and is operated as a free service to bring together clients having translation problems and language specialists in the fields of science and technology. Persons or firms needing qualified translators are invited to address inquiries to Wayne Kalenich, librarian, and translators are urged to place their qualifications on file with the directory. Twenty-three languages are already represented among the specialists listed and it is hoped that translators in all fields of knowledge will eventually be registered. Information concerning interpreters is also solicited.

The Special Libraries Association Translations Pool, also under the management of Mr. Kalenich, lists technical translations and information as to their loan or purchase. About three thousand translations have been indexed and persons planning to translate a technical article are urged to check with Mr. Kalenich to make sure that such a translation is not already available.

The National Registry of Rare Chemicals, 35 West 33rd Street, Chicago 16, has submitted the following list of wanted chemicals: 5,7,2′,3′-tetrahydroxyflavanone, 3,5,-6,7,2′-pentahydroxyflavone, 3,5,6,7,-3′,4′-hexahydroxyflavone, 3,6,2′,4′-tetrahydroxyflavone, 5,7,2′,4′-tetrahydroxyflavone, 4′-methyl-3,4-benzpyrene, 20-ethylcholanthrene, 3-chloro-20-methylcholanthrene, 6-cyano-20-methylcholanthrene, coriamyrtin, deuteroformaldehyde, 1-decalol, monodeuteroethylene, phenylpantothenone, cyclooctanone, picropodophyllin, muscarine, fructose-6-phosphate, thiomethylpentosides, cadinene, and keracyanin.

About one hundred numbers of the ***Philippine Journal of Science*** (1929 to 1941), are available to anyone willing to pay the cost of transportation. Not all volumes are complete, and articles on fishes and orchids have been extracted from a number of the issues. The publications may be obtained from Hugh Craig, Schnell Publishing Co., Inc., 59 John Street, New York City 7.

Institut International des Sciences Théoriques, of Brussels, has announced that a prize of 50,000 francs (Belgian) will be awarded for the best paper on the "Exposition and Critique of the Conceptions of Eddington Concerning the Philosophy of Physical Science." Papers must be submitted before December 31, 1950. Further information may be obtained from the Secretary, Institut International des Sciences Théoriques, 221, Avenue de Tervueren, Brussels, Belgium.

A new international journal, *Applied Scientific Research,* will be published at The Hague under the auspices of the Central National Council for Applied Scientific Re-

search in the Netherlands, the Applied Physics Section of the Netherlands Physical Society, and the Section for Technical Scientific Research of the Royal Institute of Engineers of the Netherlands. The journal will be issued in two sections: A, containing papers on applied mechanics, hydro- and aeromechanics, heat, and the mechanical and thermal properties of materials; and B, containing papers on applied electrophysics, acoustics, optics, and the electrical, acoustical, and optical properties of materials. The subscription price is 20 guilders per volume for each section. American subscribers may send their orders and remittances through Tice and Lynch, Inc., Forwarding agents, 21 Pearl Street, New York City.

An *Interim Checklist of Holdings of 168 German Medical and Dental Periodicals, 1939–1948, in 38 Libraries of the United States and Canada* has been compiled by the **Committee on Periodicals and Serial Publications of the Medical Library Association.** The number of copies to be published will be based on the number of orders received by July 15. To assure receipt of a copy, an order, accompanied by remittance of $1.00, should be sent before that date to: Mrs. Edith Dernehl, Marquette University Medical Library, 561 N. 15th Street, Milwaukee 3, Wisconsin.

The Linnean Society of New South Wales announces that the position of Macleay Bacteriologist is open to qualified researchers in agricultural bacteriology. The appointment, which carries an annual salary of £600 to £900 (Australian) is for a five-year period. Further information may be obtained from the Secretary, Linnean Society of New South Wales, Science House, 157 Gloucester Street, Sydney, New South Wales, Autralia. Applications should include three references and must be submitted to the secretary by *June 30*.

The Atomic Energy Commission has announced that limited quantities of isotopically-labeled compounds, produced in excess of AEC needs, will be made available from the Oak Ridge National Laboratory upon allocation from the Isotopes Division. The only compounds now on hand are C^{14}-labeled sodium butyrate, sodium valerate, sodium caproate, and sodium heptanoate, but other labeled compounds will be added to the list. Elemental boron[10] can also be furnished for research purposes. Inquiries should be addressed to the Isotopes Division, Atomic Energy Commission, Oak Ridge, Tennessee.

The AEC recently compiled a list of physicists, chemists, and biologists who have agreed to act as consultants on isotope techniques. This list (Isotopes Division Circular E-22) is available upon request from the Oak Ridge Laboratory.

The Growth of the Experimental Sciences, a pamphlet describing the experiment of President James B. Conant and his assistants in teaching the tactics and strategy of science to nonscience students at Harvard College, has just been published for private distribution through the courtesy of the Carnegie Corporation. Dr. Conant warns that his case-history approach is "both controversial and experimental." Copies will be mailed without charge, while the supply lasts, to any interested college professor or educational administrator on application to Guy Snavely, 726 Jackson Place, NW., Washington, D. C.

Recently Received—

Health Problems in Industry: A Digest of the Proceedings of the Joint Conference of Doctors and Businessmen, held at the Assembly Hall of the Commerce and Industry Association of New York, Inc., December 1, 1948. Available on request from the Information Service, New York University-Bellevue Medical Center, 141 Broadway, New York 6, N. Y.

Psychological Cinema Register: a nonprofit sale and rental distribution service of selected 16-mm instructional motion picture films in psychology, psychiatry, physiology and related fields, No. 6, 1949. Audio-Visual Aids Library, Pennsylvania State College, State College, Pennsylvania.

Occupational Outlook Handbook: Employment Information on Major Occupations for Use in Guidance, Bulletin 940, prepared in cooperation with Veterans Administration. Publication of the U. S. Department of Labor. For sale by the Supt. of Documents, U. S. Govt. Printing Office, Washington 25, D. C. at $1.75.

Hatchability of Chicken Eggs as Influenced by Environment and Heredity by Walter Landauer. Bulletin 262, April 1948, (revision of Bulletins 216 and 236). Storrs Agricultural Experiment Station, College of Agriculture, University of Connecticut, Storrs, Connecticut.

Journal of Calendar Reform, International Edition, First Quarter 1949. World Calendar Assn., Inc., 630 Fifth Avenue, New York 20, N. Y.

Expanding World Trade — U. S. Policy and Program. *Foreign Affairs Background Summary.* Issued by the Office of Public Affairs, Department of State, Washington, D. C.

Vegetation-Types Map of Tanganyika Territory by Clement Gillman. Available from the American Geographical Society of New York, Broadway at 156th Street, New York 32, N. Y. at $1.00 per copy postpaid.

Make Plans for—

American Society of Ichthyologists and Herpetologists, annual meeting, June 18–21, U. S. National Museum, Washington, D. C.

Inter-University High Altitude Laboratory, cosmic ray symposium, June 22–28, Echo Lake, Colorado.

Western Psychological Association, June 24–25, Eugene, Oregon.

American Physical Society, summer meeting, June 27–29, University of Washington, Seattle; meeting of the Division of Fluid Dynamics, June 30–July 1, Naval Ordnance Laboratory, White Oak, Maryland.

International Union for the Scientific Study of Population, August 27–September 3, Geneva, Switzerland.